THE OPEN UNIVERSITY
A SCIENCE FOUNDATION COURSE

UNIT 23 PHYSIOLOGY

STUDY GUIDE 3

1 INTRODUCTION AND TV PROGRAMME 3

2 OXYGEN SUPPLY 4

2.1 Diffusion of oxygen molecules 4
2.2 Oxygen supply in small multicellular organisms 6
2.3 Oxygen supply in large multicellular organisms 8
Summary of Section 2 10

3 CIRCULATORY SYSTEMS 11

3.1 Blood and oxygen transport 11
3.2 The heart and blood vessels 12
3.3 The physiological demands of exercise (Experiment) 15
3.4 Blood cells and haemoglobin 18
Summary of Section 3 20

4 REMOVING THE PRODUCTS OF METABOLISM 21

4.1 Disposal of carbon dioxide 21
4.2 Elimination of water and nitrogen compounds 22
4.3 Heat transfer 23
Summary of Section 4 24

5 SUPPLY OF GLUCOSE 24

5.1 Regulation of blood glucose levels 25
5.2 Responses to low blood glucose levels 26
5.3 Effect of high blood glucose levels 26
5.4 Hormones and the regulation of blood glucose levels 27
Summary of Section 5 27

6 CONTROL MECHANISMS 28

6.1 Control of blood glucose level 31
6.2 Control of breathing 32
6.3 Nervous control of heart beat 33
6.4 Hormonal control of heart beat 36
Summary of Section 6 37

7 CONCLUSION 38

OBJECTIVES FOR UNIT 23 39

FURTHER READING 39

ITQ ANSWERS AND COMMENTS 40

SAQ ANSWERS AND COMMENTS 41

ACKNOWLEDGEMENTS 42

INDEX FOR UNIT 23 42

STUDY GUIDE

This Unit consists of a main text and TV programme. There is one experiment (in Section 3) that should take you about 45 minutes to complete. It involves taking mild exercise (stepping on and off a step about 100 times) and measuring your pulse. No special equipment is needed—but if, for any reason, it would be unwise for you to exercise in this way, you should look for someone to act as your subject.

The TV programme shows a number of physiological measurements being made, and the experiments that you will see tie in directly with the text, notably Section 5 on glucose supply. It is not essential for you to read the text before seeing the programme, but you should read the TV notes at the beginning of the Introduction.

The Unit follows closely on from Unit 22, dealing with the way in which physiological processes provide cells with oxygen and glucose for catabolism and remove from them the products of catabolism. Although many of the detailed examples come from *human* physiology, you should pay attention to the references to other animals whose physiology is different. As well as making these physiological comparisons, the Unit refers often to the evolutionarily important theme of the relationship of structure to function: you should be aware of these (necessarily) scattered references. A further important theme of the Unit is that of physiological regulation and control. The main development of this topic is in Section 6.

1 INTRODUCTION AND TV PROGRAMME

In the TV programme 'A day in the life' you will see how physiological measurements are made. You already know something about physiological measurements from the TV programme 'Practically speaking', associated with Unit 4, and you will be measuring heart rate during your study of Unit 23. 'A day in the life' follows on from the previous programme on chemical energy, 'The fires of life', and looks at the whole organism. Measurements will be made on humans, and you should note the techniques that are used.

The programme centres on the link between food intake (type, calorific value, etc.) and energy supply for movement. The calorific value of food is measured by using a bomb calorimeter. A sample of food is completely oxidized inside a metal 'bomb', which absorbs the heat produced. From the rise in temperature of the 'bomb', the heat produced by the oxidation can be calculated.

The physiological measurements will be made on a man during his normal working day. He will be taking some exercise while the experiment is in progress. Unit 4 introduced you to the idea of control experiments, and a control will be used here. The measurements made on Sam, the exercising volunteer, will be compared with the values obtained from the sedentary narrator who will constitute the control. Both will be fed a standard meal, whose calorific value has been measured, and we will 'watch' the movement of glucose into the blood by taking blood samples at intervals. We shall monitor heart rate and measure respiration rate. You should ensure that you can make notes about the values obtained from the measurements.

Your aim is to be able to describe:

(a) how energy is derived from food;
(b) how blood glucose levels vary during the day;
(c) how the circulatory system performance is matched to demand;
(d) what the limits on human performance are.

PHYSIOLOGY

In Unit 22 you were introduced to the biochemical processes that generate usable energy, in the form of ATP, by breaking down carbohydrates and other compounds in a controlled manner. As most of these cellular reactions are overall oxidations, we need to ask: how do organisms obtain oxygen from their environment and convey it to the mitochondria deep within the cells? A similar question should be asked about the nutrients: how is what a lion eats, or what a plant makes in its leaves, delivered in the correct chemical form to the catabolic enzymes of the energy-requiring cells? Turning to the products of catabolism, the ATP that is formed is rapidly reconverted to ADP and P_i as it is used in cellular reactions. But what of the 'waste products'—water, heat, carbon dioxide and, if amino acids are the fuel, the various compounds of nitrogen—how are they removed from the organism? In addition to the relatively simple questions of reactants and products, there is the product of *regulation* and *co-ordination*. Sleeping and running pose very different demands in terms of the supply of fuel and oxygen and the disposal of waste. How is each of these controlled? The Unit deals with these questions, sometimes very briefly and sometimes in detail. In so doing, it ranges from looking at small simple animals to considering the lungs, heart and kidneys of larger ones.

The study of function in living organisms is called **physiology**, a word that comes from the Greek meaning 'knowledge of natural things'. This term has been in use for about 200 years but, as the study of nature has broadened in the 20th century, physiology has become restricted in meaning. It may now be defined informally as the study of how animals and plants work. You will see shortly that physiology makes considerable use of physics and, in particular, classical mechanics to account for what is observed in living systems. This should not be very surprising since you known by now that there is no need to invoke a separate unique 'vital force' to distinguish between what is inert and what is alive. One can wonder at the diversity and complexity of nature, but nature must conform to the same physical laws as everything else in the Universe. Let us apply this kind of approach to the 'supply and disposal' problems noted above—beginning with oxygen.

2 OXYGEN SUPPLY

In Unit 22, Section 2.3 you were introduced to the idea that almost all organisms depend on oxidative reactions to provide them with usable energy in the form of ATP. Heterotrophs oxidize food they have eaten; autotrophs oxidize the organic compounds that they have made for themselves—usually by photosynthesis. The overall equation for this oxidation is:

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O + \text{energy} \qquad (1)$$

How is oxygen 'captured' from the environment and delivered to the mitochondria in the right quantities to sustain this reaction?

2.1 DIFFUSION OF OXYGEN MOLECULES

As you might expect, the way in which oxygen is delivered to cells varies from one organism to another—fish are different from worms, and single-celled organisms are different from locusts, which in turn are different from humans. However, there is a common starting point—the oxygen in the Earth's atmosphere. The layer of air seven miles deep, dense at ground level and progressively thinner as altitude increases, contains about 20% of oxygen by volume; the rest is mainly nitrogen. This means that at sea-level in one litre of air there is about $200\,cm^3$ of oxygen—a concentration of $200\,cm^3\,l^{-1}$. In biological terms, this is a rich source of supply: around $5\,m^3$ of air will provide enough oxygen molecules to catabolize all the food you eat in a day. Where the supply problem arises, however, is in the extraction of oxygen from the air and the delivery of it to the cells that need it.

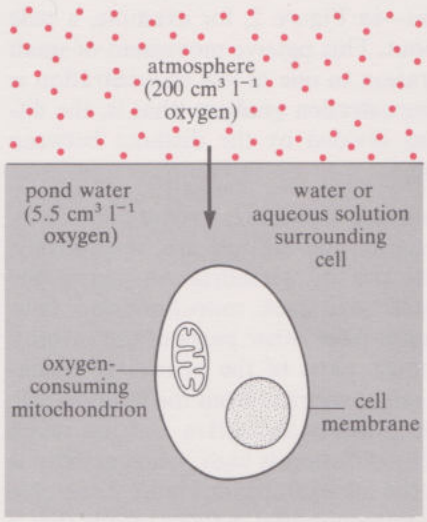


FIGURE 1 Oxygen capture from a gaseous mixture and transport to a solution within a single-celled organism.

The mechanisms for oxygen capture and transport that have evolved are many and varied, but there are underlying features common to all organisms: all involve the movement of gaseous oxygen molecules from the air, via a solution outside the cells to solution in the cytosol within the cells. With this kind of route, which is illustrated for a single-celled organism in Figure 1, various physical difficulties have had to be overcome in the course of evolution—and chief among these is the relative insolubility of oxygen in aqueous solution.

For aquatic organisms, the significance of solubility is plain. Although the atmosphere contains a high concentration of oxygen (about $200\,cm^3\,l^{-1}$), the oxygen content of natural waters is very much less, varying from almost zero in stagnant waters to a maximum of about $10\,cm^3\,l^{-1}$.

> Using your general knowledge of rivers and seas around the world, what do you think could account for such variation?

One factor is temperature. As the temperature rises, so the amount of gas in solution falls: at 30 °C freshwater only contains $5.5\,cm^3\,l^{-1}$ oxygen, whereas at 0 °C it contains almost twice as much. Thus the cold waters of the Arctic are comparatively rich in oxygen and, partly for this reason, contain a large quantity of organisms. The solubility of oxygen is also influenced by the amounts of other solutes present: salts in solution reduce the concentration of oxygen dissolved in seawater to about three-quarters of that present in freshwater at the same temperature. Pressure also has a marked effect: at high altitudes, where atmospheric pressure is low, the concentration of dissolved oxygen is also lower than it would be at sea-level.

But, whatever the nature of an organism's environment, a significant part of the route travelled by the oxygen molecules as they journey from environment to mitochondria will be in solution, as you have seen in Figure 1. This is as true for terrestrial animals as for aquatic ones and, indeed, is also true for plants.

In any solution, the molecules of solute and solvent (Units 13–14, Section 6.1) are in continuous motion. The motion is random, with frequent collisions between molecules. If coloured solute molecules are used, such as those of red ink in Figure 2, you can see that the solute molecules migrate from regions of high solute concentration to regions of lower solute concentration. If left until a stable state is reached, the solute concentration would

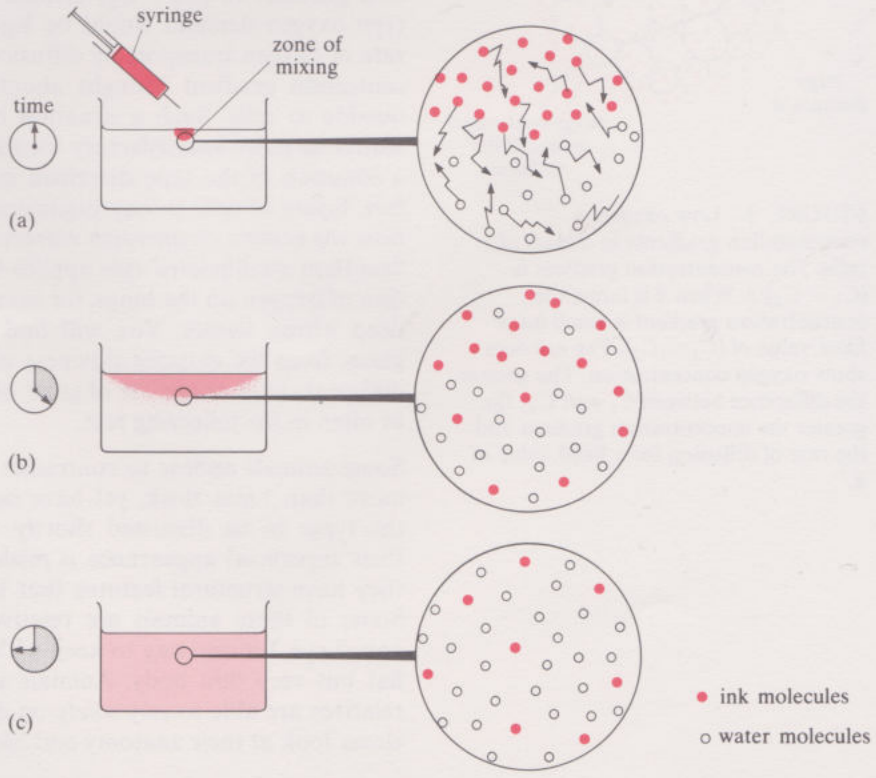


FIGURE 2 An example of diffusion. When a droplet of ink falls on to the surface of water in a container, the ink gradually disperses throughout the water. This is the result of the random movement of molecules (shown by the arrows in (a)). Water molecules gradually pervade the ink drop, and (over time) ink molecules spread out into the water ((b) and (c)).

DIFFUSION

CONCENTRATION GRADIENT

EXTRACELLULAR FLUID

be the same in all parts of the solution—in Figure 2, for example, a pale pink solution of ink molecules throughout. This passive movement of small molecules from a zone of high concentration to one of low concentration is called **diffusion**—and the greater the **concentration gradient** (that is, the difference between the two concentrations divided by the distance between them), the greater is the rate of diffusion.

This has important consequences for oxygen transport, as you can see by looking again at Figure 1. Here the solute and solvent are, respectively, oxygen and water. When the cell respires and mitochondria use oxygen, the concentration of oxygen in the cytosol near each mitochondrion falls. Oxygen molecules diffuse into those zones from other parts of the cytosol, and—in like manner—the oxygen in those parts of the cytosol is replenished by diffusion of oxygen across the cell membrane from the fluid outside the cell (**extracellular fluid**). When mitochondria are active and use much oxygen, the rate at which it is replaced by diffusion is high; when activity is lower, the rate of diffusion is slower. In the ink example in Figure 2, a stable state is eventually reached. Continuous mitochondrial activity means that a stable state—an even concentration of oxygen—never occurs in the cell.

This description of oxygen diffusion into cells is almost the complete story of oxygen supply for unicellular organisms. A single cell needs only a small amount of oxygen, in absolute terms, and the distance the oxygen has to travel is small. Oxygen enters the cell through the membrane fast enough to provide oxygen for all the oxidative reactions. In organisms made up of many cells, the distance over which the oxygen must diffuse is potentially greater. As you will see, the problem is solved in different ways.

2.2 OXYGEN SUPPLY IN SMALL MULTICELLULAR ORGANISMS

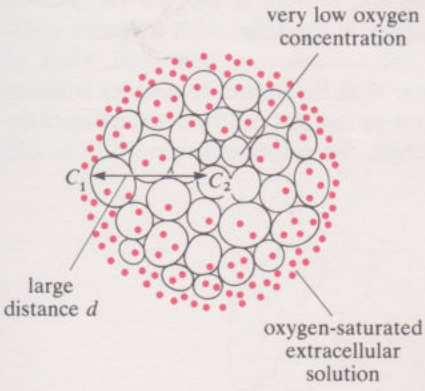


FIGURE 3 Low oxygen concentration gradients in a mass of cells. The concentration gradient is $(C_1 - C_2)/d$. When d is large, the concentration gradient is small for a fixed value of $(C_1 - C_2)$. The red dots show oxygen concentration. The greater the difference between C_1 and C_2, the greater the concentration gradient and the rate of diffusion for a fixed value of d.

Imagine now a small multicellular organism consisting of a lump or a few layers of cells. Because of increasing distances from the oxygen-containing outside environment to oxygen-requiring mitochondria, the concentration gradients involved become much lower. You can see this clearly in Figure 3: here the oxygen concentration at the margin is C_1 and that at the core of the lump is C_2, and the distance between the two is d, giving a concentration gradient of $(C_1 - C_2)$ divided by d. Hence, in a mass of cells of this type oxygen demand would be *high* because there are many cells, yet the rate of oxygen transport by diffusion would be *low* because of the low concentration gradient brought about by the relatively great distance from outside to cells. Such a situation of high demand and inadequate supply would be most unsatisfactory for the organism, and it is not surprising that a situation of the type described in Figure 3 does not occur in nature. In fact, layers of cells in any organism *are never more than about a millimetre from the nearest oxygen-rich extracellular solution*—and, as you will see, this 'less than a millimetre' rule applies both to cells concerned with the acquisition of oxygen (in the lungs, for example) and to those that consume oxygen deep within tissues. You will find that this 'rule'—arising, as you might guess, from the extreme slowness with which oxygen molecules are able to diffuse through water—is of great biological importance and will be referred to often in the following text.

Some animals appear to contradict this rule in that they *look* as if they are more than 1 mm thick, yet have no special oxygen-transporting system of the types to be discussed shortly. However, close inspection reveals that their superficial appearance is misleading. Careful examination shows that they have structural features that keep diffusion distances less than 1 mm. Some of these animals are relatively easy to find and observe with the naked eye, for one way to keep within the 1 mm limitation is to have a very flat but very thin body. Animals such as tape-worms and their flatworm relatives are able to rely *solely* on diffusion for their oxygen supply—and a closer look at their anatomy and life-style shows how they can do this.

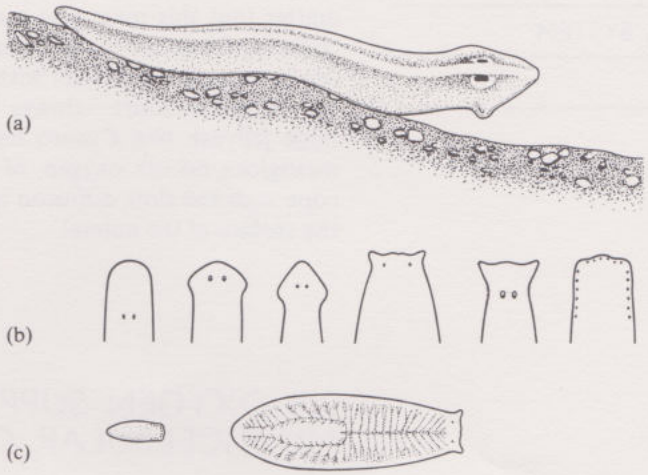


FIGURE 4 (a) A flatworm. (b) The heads of different flatworms that are found in ponds and streams. The position and number of eyes varies with the species. A number of the common species are shown here. (c) The actual size of a typical small and a large flatworm. The thickness (into the paper) is about 0.5 mm.

Flatworms (Figure 4) are found in almost every kind of freshwater from small pools to very cold mountain streams. They can also be found on the sea-shore in rock pools, and some are even terrestrial though restricted to damp areas. If you have some freshwater near you—a river, pond, or canal—go and look for flatworms. They are found on the undersides of stones (often in large numbers), on floating leaves or on submerged plants such as mosses. When still, they look like irregularly shaped lumps of jelly, but when extended they are up to 4 cm long and about 1 cm wide. Their colour can vary from white through all the shades of brown to black. Don't confuse them with the small harmless leeches which are superficially similar but have a sucker at each end. If you remove flatworms gently from the stone or leaf and place them in a glass container of fresh water, after a few minutes they should extend and start to move. They often glide with no apparent muscular movement, using very fine hairlike projections called cilia on the undersurface. They can glide upside down on the surface of the water, supported by the surface tension. You will meet cilia again in other animals, performing different functions, because cilia are widespread in animals from single-celled organisms to humans.

Most flatworms are around 0.5 mm thick. Can you suggest why flatworms don't grow up to the maximum thickness of 1 mm mentioned earlier?

As flatworms usually have one surface in contact with the 'ground', only half the body area is available for the uptake of oxygen. Therefore the maximum thickness is about half the theoretical maximum value.

Having a flat body is not the only way in which an animal can have dimensions that exceed 1 mm while keeping all cells less than 1 mm from an oxygen supply so that diffusion can take place. Look at the jellyfish in Figure 5a. At first sight it seems impossible that such a large organism could manage to obtain oxygen by diffusion alone. However, if we were to take a slice out of the animal (Figure 5b), we would see that the rather thick central mass of jelly-like tissue *has very few cells* in it—and so it does not



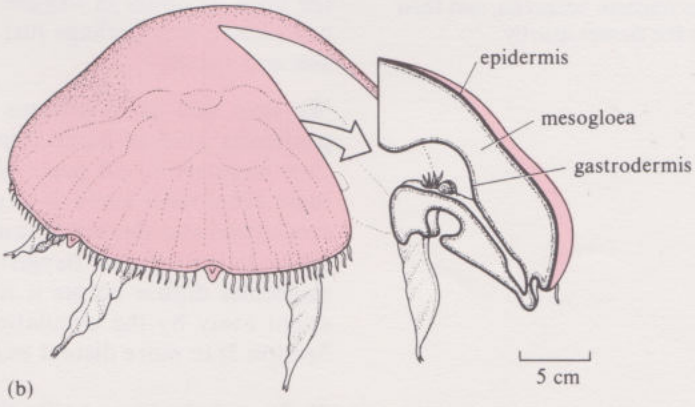


FIGURE 5 (a) *Cyanea*, a jellyfish. (b) Section of a jellyfish to show the two tissue layers, and the mass of jelly in the centre. The epidermis is a single layer of cells lining the surface. The gastrodermis is a single layer of cells lining the digestive cavity.

TRACHEAL SYSTEM

SPIRACLE

ALVEOLI

matter that this mass (the mesogloea) is so far from oxygenated water. In contrast, however, the two single layers of cells surrounding the mesogloea are in continuous contact with the water. This means that the diffusion path for oxygen is short—always less than a millimetre—despite the fact that large jellyfish like *Cyanea* may grow to 3 m across! The cells within the mesogloea do use oxygen, of course, but at such a low rate that they can cope with the slow diffusion rate that results from their large distance from the surface of the animal.

2.3 OXYGEN SUPPLY IN LARGE MULTICELLULAR ORGANISMS

There are, however, a limited number of variations on the flatworm and jellyfish theme and all of them involve either thin or 'frilly' organisms in which the environmental oxygen is never very far from the layer of cells. Yet there is a very large number of species of relatively big and compact organisms that are clearly not constrained in size by the need to keep their cells within 1 mm of *the outside environment*. All of these, however, continue to ensure that all cells are within 1 mm of an *internal* fully oxygenated solution. This is achieved, depending on the type of animal, in several different ways; two are discussed below.

(i) In insects, air is taken into the animal and 'piped' by a system of tubes to every part of its body. No cell, therefore is more than 1 mm from the end of an air tube.

(ii) In others, mammals, birds and fish, for example, oxygen is taken from the environment into a fluid medium within the body, and this oxygen-containing *liquid* is circulated to within 1 mm of the cells that need oxygen.

Let us consider each of these in turn.

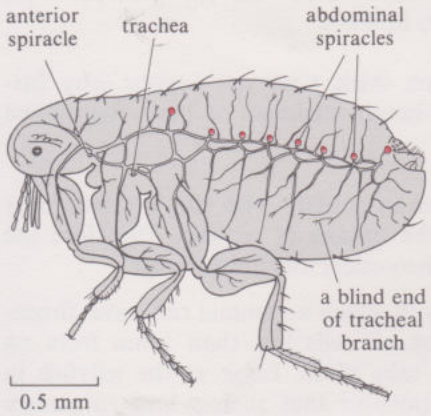


FIGURE 6 A side view of a flea, showing the internal tracheae that carry oxygen to the tissues from the spiracles. Oxygen goes into solution at the blind ends of the tracheal branches, and then diffuses to the tissues nearby.

Insects are unusual in having a distribution system for air. Most animals, as noted above, use a circulating liquid to carry acquired oxygen. In insects, however, oxygen reaches the tissues by a system of tubes that carries the air itself through their bodies (Figure 6). This tube system is called the **tracheal system**. The tracheae open to the atmosphere through valves called **spiracles**. In small insects, air movement may be passive, but, in most, muscles contract to force air in and out of the tubes. The main tracheae have side trunks that in turn have many branches. The ends of the tracheae are very small and are very permeable to water. Most oxygen diffusion into the tissues takes place at these blind ends. Despite the anatomical complexity of the tracheal system, the underlying principle is the now familiar one of ensuring that the diffusion pathway is short.

This system of tubes provides a very efficient way to distribute oxygen to the cells in small insects. But in very active insects (the house-fly has a wing speed of about 120 beats per second), the rate at which the flight muscles consume oxygen is so great that there is an upper limit on the size of flying insects imposed by the rate at which an internal tube system can provide the huge amounts of oxygen needed. Considering the success of insects on our planet, it is perhaps just as well for us that there is an upper limit on size and speed!

We turn now to organisms that use specialized systems to oxygenate a particular kind of liquid (blood, as you will see in Section 3), which they then circulate to all parts of their bodies. Across the range of organisms there are several kinds of oxygenating organs—gills and lungs are the most specialized and the best known. Both involve exposing a *large area* of membrane to the external oxygen-rich environment, with the result that oxygen molecules diffuse across it into the underlying blood supply. This is then swept away by the circulation system (again, you will see more of this in Section 3) to more distant parts of the body.

☐ How do lungs and gills differ as regards oxygen source?

■ For organisms with gills, the oxygen-rich external environment is water. Thus diffusion occurs directly from the environment, across the gill membranes, into the blood. Organisms with lungs have air as the oxygen-rich external environment. This dissolves in the surface water on the external surfaces of the lung membrane. Thereafter, the route is as before—diffusion from the solution across the membrane into the circulating blood.

Lungs have, therefore, to capture atmospheric oxygen so that it will dissolve in water before it can enter the body by diffusion. How do they do this?

Unit 22 introduced you to the idea of respiration being the catabolic breakdown of sugars and other carbon compounds to provide energy. Physiologists, however, sometimes use the word respiration to mean the physical *process* of breathing (from the Latin *spirare*, 'to breathe'). The respiratory system in humans consists of the nose, mouth and lungs, together with the tube that links them: the trachea. During breathing, air is taken in through the nose or mouth and passes down the trachea to the lungs. Each lung consists of a series of branching tubes, each tube getting narrower at each branch. The smallest thin-walled tubes, the **alveoli**, are the sites at which oxygen diffuses into the blood. This arrangement is shown in Figure 7a. In Table 1, the sizes of the component tubes of the lung are compared, and the approximate number present in each lung is shown. The contribution of each to the total volume of air held in the lung is given (as a percentage) in the last column. You can see that 70% of the air in the lung is within the alveoli, where oxygen absorption takes place.

TABLE 1 The numbers and sizes of the tubes of the human respiratory system and the volumes of air held within them.

	Number	Diameter/mm	Volume/%
Trachea	1	18	1.7
Small bronchi	10^3	1.3	2.3
Bronchioles	10^4	0.8	3.0
Respiratory bronchioles	3×10^5	0.5	23
Alveoli	3×10^8	0.1	70

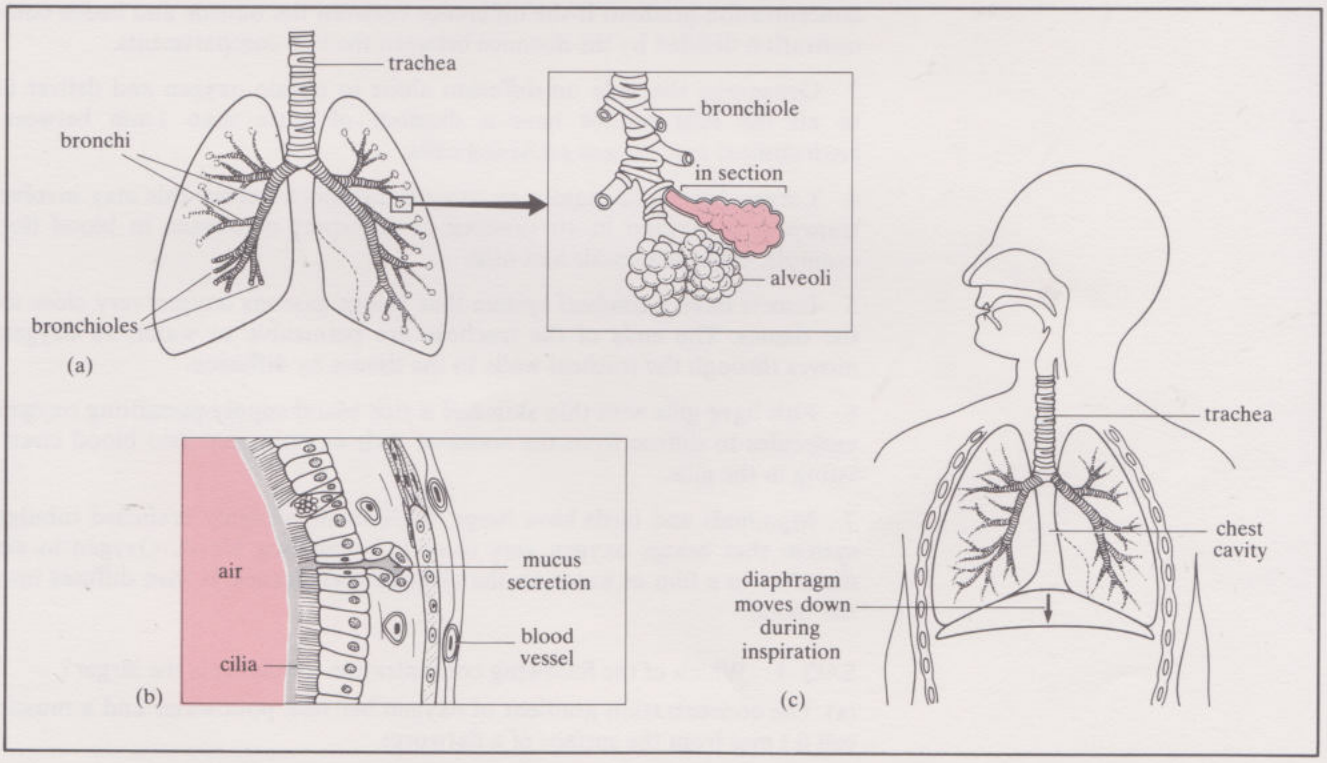


FIGURE 7 Lung structure. (a) The structure of the human lung. (b) The cells that line the bronchi, showing the cilia that remove dust and other small particles, and the cells that produce the mucus. (c) The position of the lungs in the chest cavity of a human, showing how the diaphragm moves during inspiration.

PLASMA

HAEMOGLOBIN

It is interesting to note that the air that is taken into the lungs may well contain small particles of dust that could block the alveoli. These need to be disposed of, and in the bronchioles and bronchi (singular, bronchus) there are cells with small hairs projecting from them (see Figures 7a and 7b). The hairs, called cilia, propel particles along; they are similar to the hairs that propel flatworms (Section 2.2). In the bronchioles, cilia move dust particles away from the alveoli towards the bronchi. The particles are then caught up in a sticky fluid called mucus, and it is this mucus that causes us to cough when it reaches the trachea.

The movement of air into the lung is accomplished by the muscles in the chest—in fact, the same muscles that are involved in coughing. Separating the chest from the abdomen is a muscular membrane called the diaphragm. During quiet breathing, that is when no exercise is being performed, contraction of the diaphragm muscles alters the shape of the diaphragm and it draws air into the lungs. When contraction ceases, the elasticity of the chest and lungs restores the diaphragm to its original shape and the lungs expel air (Figure 7c). During exercise, the chest muscles and the diaphragm help to draw in and expel air. The result of this movement is that there is a tidal flow of air into and out of the alveoli: a resting person inhales 5 litres of air per minute. As a consequence, fresh supplies of air are continuously being brought into contact with the $100\,m^2$ of alveolar surface available for gaseous exchange. Blood in vessels beneath the alveoli (Figure 7b) becomes oxygenated as a result of diffusion across the walls of the alveoli and blood vessels—the diffusion distance is, as ever, small. What happens to the oxygen as it enters the blood within the lungs is a separate question that is considered in Section 3.

SUMMARY OF SECTION 2

1 Oxygen from the air dissolves in water. Small aquatic organisms can absorb this oxygen and pass it directly to all of their cells by diffusion alone.

2 The rate of diffusion of oxygen into an organism is proportional to the concentration gradient between the outside and inside of the organism. The concentration gradient is the difference between the outside and inside concentration divided by the distance between the two compartments.

3 Organisms that rely on diffusion alone to obtain oxygen and deliver it to all the cells cannot have a distance of more than 1 mm between environment and oxygen-requiring cells.

4 Larger organisms require an oxygen transport system: this may involve transport of oxygen in air (insects) or transport of oxygen in blood (for example, birds, mammals and fish).

5 Insects have a tracheal system that brings gaseous oxygen very close to the tissues. The ends of the tracheae are permeable to water, so oxygen moves through the tracheal walls to the tissues by diffusion.

6 Fish have gills with thin skin and a rich blood supply permitting oxygen molecules to diffuse from the water of their environment into blood circulating in the gills.

7 Mammals and birds have lungs that contain a highly branched tubular system that brings oxygen very close to circulating blood. Oxygen in air dissolves in a film of water on the alveolar membranes. It then diffuses into the blood.

SAQ 1 Which of the following concentration gradients is the larger?

(a) The concentration gradient of oxygen between pondwater and a muscle cell 0.1 mm from the surface of a flatworm.

(b) The concentration gradient of oxygen between the same pondwater and an identical muscle cell 0.25 mm from the surface of a flatworm.

SAQ 2 Which of the following rates of oxygen diffusion is likely to be greater?

(a) The rate of diffusion from pondwater into a rapidly metabolizing cell 0.3 mm from the surface of a flatworm.

(b) The rate of diffusion from the same pondwater to a cell with very few mitochondria 0.3 mm from the surface of a flatworm.

3 CIRCULATORY SYSTEMS

Section 2 established that in large animals the supply of oxygen to each cell is not possible by passive means because the distances involved are too great. Diffusion alone would give an impossibly slow rate of oxygen transport. Thus, many animals have circulatory systems that move fluid containing oxygen to various parts of the body. The one that you will be most familiar with is the flow of blood in your own body.

> Blood has many functions, some of which you should already know, both from this Unit and from general knowledge. List as many as you can.

From what has been said already, oxygen transport is probably at the top of your list. Then, from what you know of catabolism from Unit 22, you might also have mentioned transport of glucose, fats and amino acids from the intestine to (ultimately) the cells where they are catabolized as fuel. From your knowledge of these catabolic reactions, you might have mentioned the transport of carbon dioxide, which is produced in cells and transported back to the lungs by the blood and thus eliminated. Two additional important functions that you may not be aware of will be discussed later in this Unit: the *circulation of hormones*, and the *movement of heat*. In addition, there are other functions not discussed in this Course, such as the crucial role of the blood in the body's defence mechanisms.

In this Section we shall be looking at the structure and function of the circulatory system—paying particular attention to the delivery of oxygen to metabolically active cells. Other functions of the blood—heat transport, removal of CO_2 and other products and the provision of glucose as fuel—are covered in Sections 4 and 5.

3.1 BLOOD AND OXYGEN TRANSPORT

At the end of Section 2, you read about the function of the lungs in humans. You saw how the airways in the lungs branch extensively and become narrow with the result that, at the alveoli, the diameter is only 0.1 mm, and only a very short diffusion path separates air from the blood. As a result, oxygen molecules diffuse rapidly from the solution on the surface of the alveoli, across two layers of cells (alveolar membrane and wall of blood vessel), to the watery fluid (**plasma**) of blood.

As you will see in Section 3.4, blood can carry substantially more oxygen (fifty times as much!) than would be possible if the oxygen were in simple physical solution. The reason is that red blood cells, suspended in the plasma, contain the complex protein, **haemoglobin**. This combines (reversibly) with the oxygen entering the blood vessels from the alveoli—thus decreasing plasma oxygen concentration, so allowing more oxygen to diffuse in. The oxygen-laden haemoglobin is carried away by the circulatory system to the tissues where, through the reversibility of the reaction, the oxygen is released and made available to the respiring cells.

Before we turn to the functioning of the human circulation system (in Section 3.2), it is worthwhile reminding ourselves that physiology is as diverse as the animal kingdom. For example, not all animals have haemoglobin as an oxygen-carrying molecule. Snails, squid, lobsters and their

TABLE 2 The oxygen consumption of several animals

	Oxygen consumption/ $cm^3 g^{-1} min^{-1}$
sea anemone	2.3×10^{-4}
earthworm	1.0×10^{-3}
octopus	1.5×10^{-3}
frog	2.5×10^{-3}
butterfly (resting)	1.0×10^{-2}
human (walking)	3.6×10^{-2}
mouse (resting)	4.2×10^{-2}
human (running)	5.1×10^{-2}
sparrow	0.1
mouse (running)	0.330
butterfly (flying)	1.7

relatives have another pigment rather similar to haemoglobin called **haemocyanin** in their blood. The blood is colourless when deoxygenated, but greeny-blue when carrying oxygen—very different from the change from dark purple-red to bright red in haemoglobin. In Table 2 some common animals are listed in increasing order of oxygen usage. Clearly, the transport systems of some organisms must be able to meet very large demands for oxygen, whereas in others demand will be much less. As you know from Unit 21, unless some phenotypic characteristic offers a real advantage in terms of relative fitness, evolutionary change will not occur. Being able to transport oxygen at the rate achieved by a mouse is not likely to be advantageous to a sedentary snail—and it is not at all surprising that haemocyanin is able to carry much less oxygen than haemoglobin. The argument can be equally well put in converse form—the high-capacity oxygen transport systems of mammals and birds appear to be adaptations to their active modes of life.

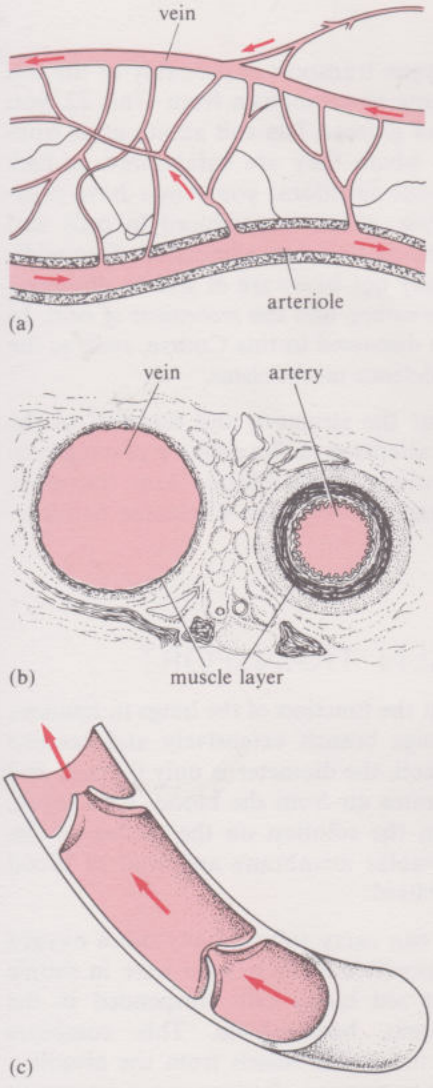


FIGURE 8 Blood vessels. (a) A network of blood capillaries connecting an arteriole to a small vein. The arrows show the direction of blood flow. (b) Cross-sections through a vein (left) and an artery (right) to show the difference in thickness of their walls. (c) A vein cut open to show the valves inside that ensure that flow is in one direction only.

3.2 THE HEART AND BLOOD VESSELS

The circulatory system of mammals (including humans) is a closed system with a pump—the heart. Tissues needing blood are penetrated by a network of small diameter blood vessels called **capillaries** (Figure 8a). The extremely thin walls of the capillaries allow the exchange of dissolved gases and nutrients between the blood and the cells. Blood enters the capillary network through small arteries called **arterioles**, and the latter receive blood direct from the heart via **arteries**. Blood is conveyed away from the capillaries back to the heart by **veins**. As Figure 8b shows, the walls of arteries are much thicker and more muscular than those of veins. Veins, however, are well supplied with valves that ensure blood flow is all in the same direction (Figure 8c). The vessel with the greatest resistance to flow is a capillary. The smaller the diameter of a tube, the greater its resistance to fluid flow, and the capillaries are the blood vessels with the smallest diameter. However, the proliferation of the capillary network away from an arteriole means that the overall cross-sectional area of the capillary network is greater than that of the arteriole that supplies it, and so has a lower resistance to flow than the arteriole. Thus it is the arteriole that provides the principal resistance to flow.

An average adult has a blood volume of around 5 to 6 litres (roughly 10 pints). When a person is exercising energetically, the output of blood from the heart, known as **cardiac output**, can be as much as $25 l min^{-1}$. This impressive value (it is about 40% greater than the delivery rate of a petrol pump on the garage forecourt!) sounds enormous, until you realize that the muscles *need* a flow rate of that level to provide sufficient oxygen for catabolism when working hard. This rate of delivery of blood is provided by a pump weighing around 300 g which can run without pause for more than 100 years in those people who reach extreme age—a remarkable organ.

Figure 9a shows the route taken by blood through the heart. You will find it useful to study this Figure carefully while you read the following text.

The heart itself is principally composed of muscle, and you can see this very clearly in the photograph of a pig's heart in Plate 9. It has four chambers, and two streams of blood pass through the heart simultaneously. The two left chambers are completely separated from the two right ones. The **atria** act principally as reservoirs for incoming blood and pump it into the **ventricles**. The ventricles are the pumps proper. Note that 'left' and 'right' always refer to the orientation of the heart (or any organ) when it is in the body. Thus the terms are independent of the way we view it—and sometimes makes diagrams of the heart confusing at first sight. In Figure 9 the heart is viewed from the front, so the left ventricle is on the right of the diagram. The same orientation applies in the photograph in Plate 9.

When blood leaves the capillaries of the tissues in the various parts of the body, it is collected by veins and channelled back to the heart, arriving at

HAEMOCYANIN
CAPILLARIES
ARTERIOLES
ARTERIES
VEINS
CARDIAC OUTPUT
ATRIA
VENTRICLES
VENA CAVA
PULMONARY CIRCULATION
DOUBLE CIRCULATION

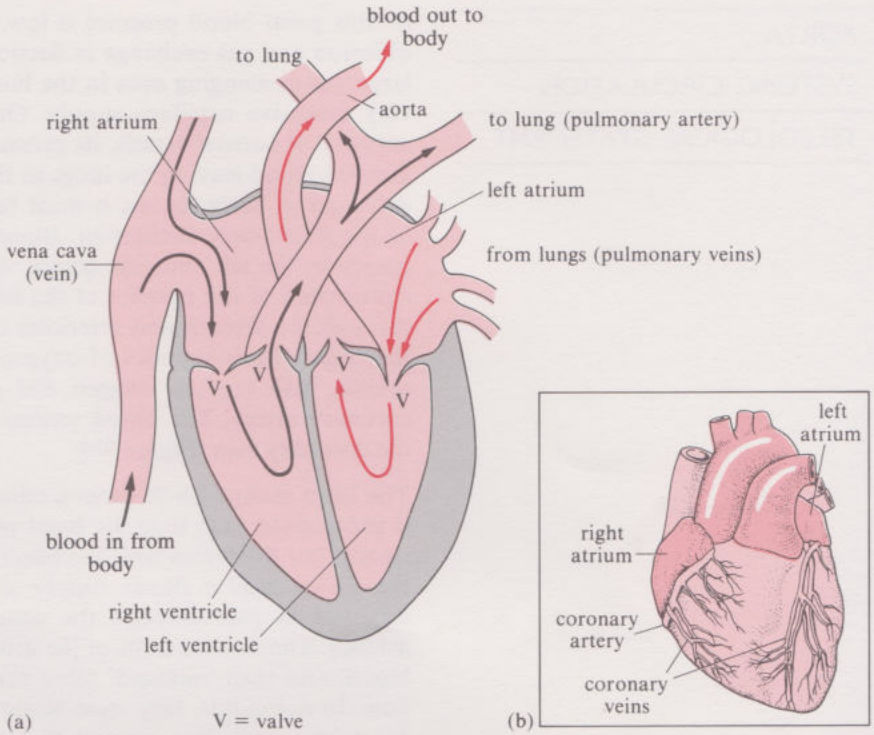


FIGURE 9 (a) A human heart viewed from the front. The heart has been cut open to show the internal structure, including the valves that ensure that blood flow is in the right direction. The red arrows show the movement of oxygenated blood through the left side of the heart, and the black arrows the movement of deoxygenated blood. (b) An intact human heart showing the coronary blood vessels. These supply blood to the heart muscle, which needs a constant supply of oxygen and metabolites as it is always working.

the right atrium via the **vena cava**. A modestly powerful contraction of the right atrium then forces blood into the right ventricle which, consequently, expands. (Back-flow is prevented by the valves you saw in Figure 8c.) This is followed by a powerful contraction in the thick muscular walls of the right ventricle, and the pressurized blood is forced along the pulmonary arteries to the lungs and through the arterioles forming part of the **pulmonary circulation** to the capillaries of the alveoli. Note that back-flow of the blood into the right atrium as a result of the contraction of the ventricle is prevented (except in those with certain heart defects) by a further set of valves between the two right-hand chambers.

Look at Figure 10 and you will see that the part of the **double circulation** so far discussed is shown by black arrows—denoting the route of deoxygenated blood. The pulmonary circulation takes blood through the lungs where gas exchange takes place: carbon dioxide, carried there by blood from the tissues, passes *into* the alveoli; the oxygen passes *out* of the alveoli into the blood ready for transport (via the heart) to the tissues.

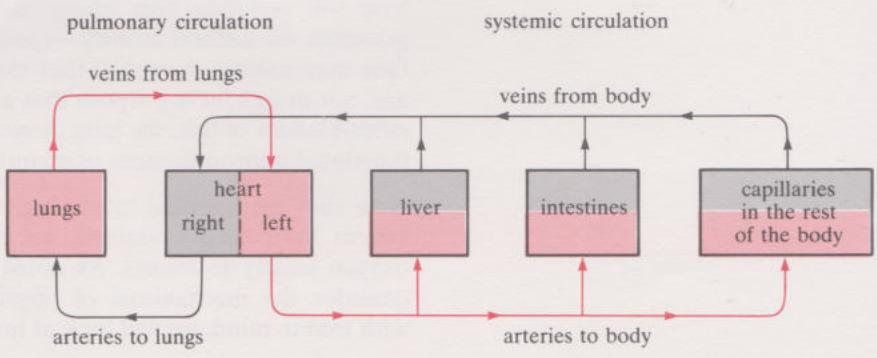


FIGURE 10 The double circulation of blood through the human heart. Oxygen-rich blood is shown as red arrows, deoxygenated blood as black arrows.

AORTA

SYSTEMIC CIRCULATION

TELEOLOGICAL STATEMENT

At this point blood pressure is low. If you think back to the discussion of diffusion and gas exchange in Section 2.3, you will appreciate that the very large gas-exchanging area in the lungs ($100\,m^2$ was cited earlier) requires a very extensive capillary supply. Once blood has passed through such a network of narrow vessels, its pressure is necessarily low. If the freshly oxygenated blood leaving the lungs in the pulmonary veins is to be successfully delivered to body tissues, it must be re-pressurized—hence the return part of the pulmonary circulation. Blood re-enters the heart at the left atrium, passes to the left ventricle (again via valves) and, by dint of the powerful contraction of the muscles of the left ventricle, is forced out, via the **aorta**, through the arteries and arterioles of the **systemic circulation** to the tissues that await fresh supplies of oxygen and glucose. The heart, being mostly muscle, also requires oxygen and glucose, and it receives blood via the coronary artery. The blood returns to the chambers of the heart through the coronary vein (Figure 9b).

The heart pumps 50–75 times a minute in a resting human adult. The blood is pressurized each time the heart pumps, so the flow from the heart is not steady, but fluctuates with the heart beat. Despite this uneven heart output, the tissues need a steady supply of blood to work efficiently—and this is achieved in part through the considerable elasticity of the walls of the arteries. The flexible walls of the arteries expand as the heart pressurizes the blood, and then 'rebound' when the pressure reduces, thus smoothing out flow. In doing this, they *store* strain energy (Unit 9, Section 2.3) during the heart beat, and then convert the stored energy to kinetic energy (Unit 9, Section 6), which is transferred to the passing blood between beats. To reduce unnecessary strain on the heart, one might have expected large arteries with consequently low resistance would have arisen through evolution. However, large arteries would entail transport of a large mass of blood—putting strain upon the pump in yet another way. In fact the outcome is a compromise—reflecting, probably, the situation that confers the greatest fitness.

Both these points, elasticity and internal diameter, are examples of the strong relationship between structure and function that one sees at all levels of biology. In physiology, this relationship is often so strongly apparent that so-called **teleological statements** are easily made. 'Alveoli have a large surface area *so that* they can exchange gases readily' is an example that you will appreciate from Section 2.3. A teleological statement is one that implies design for a *purpose*, and you should avoid writing in this way as it is, however convenient, biologically incorrect.

☐ What should you write instead of 'arteries are elastic in order to smooth out the pulses of pressure from the heart'?

■ You need something of this type: 'it is likely that smooth blood flow as a consequence of flexible artery walls has proved evolutionarily advantageous'. Or, more briefly: 'blood flow is smooth because artery walls are flexible'.

In fact, many biologists do write teleological statements as a matter of convenient shorthand: you may find some have slipped through in these Units! You will certainly hear plenty in various open network television programmes on natural history—spoken, often, by quite eminent biologists! One may assume, however, that they *are* aware that it is natural selection and not design for a purpose that accounts for the marvel of the buoyancy swim-bladder of fish, the long insect-catching tongue of a chameleon, or the functional appropriateness of mammalian double circulation.

Now that the essential 'plumbing' arrangements of the human circulatory system have been examined, we can return to the continuing theme of oxygen supply to tissues. As noted earlier, a major aim of the Unit is to consider the mechanisms of physiological regulation and control—and, with that in mind, we will look at human response to mild exercise.

3.3 THE PHYSIOLOGICAL DEMANDS OF EXERCISE (EXPERIMENT)

In the following experiment you will investigate what happens to the heart and circulatory system during exercise. To do this you either need to make observations on yourself, or persuade some *fit and healthy* friend or relative to be your subject.

If, for any reason, it would be unwise for you to exercise in the way described below, you should look for someone to act as your subject.

EXPERIMENT

INVESTIGATING THE EFFECT OF EXERCISE ON THE HUMAN HEART RATE

TIME

This experiment takes about 45 minutes

NON-KIT ITEMS

A stop-watch or clock that displays seconds.

Your body (or that of a fit subject)

A step to provide exercise for you or your assistant.

KIT ITEMS

None required for this experiment

You will be measuring heart rate by taking your pulse or that of your subject, before, during and after a period of exercise. Before starting the experiment you will need to practise taking your own pulse. You should read through the complete experiment before you start, since you will need to decide on the amount of exercise to take and also to prepare a Table in your Notebook in which to enter the results.

PRACTICE SESSION

Find the pulsating blood vessel passing over the bone of your wrist in the position shown under the middle fingers in Figure 11. (Use your fingers, not your thumb.) You may well need to press quite hard, and you will probably find it a little difficult at first. Once you are quite sure that you can feel the pulse reliably, sit in a position where you can conveniently carry out the timing. You are going to measure your own resting pulse rate.

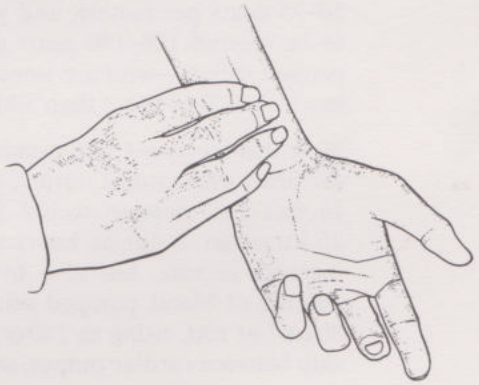


FIGURE 11 How to take your pulse.

Start the stop-watch (or look at the clock). Feel a pulse and at a convenient position of the second-hand begin to count. Stop the watch (or read the clock) when you have counted thirty-one beats of the pulse. Record the time taken for 30 beats. Heart rate is normally recorded as 'beats per minute', so you should express the time for 30 beats as the equivalent number of beats per minute. If you are unsure how to do this, try ITQ 1.

ITQ 1 Suppose that the time taken for 30 beats is 40 seconds. What is the equivalent heart rate in beats minute^{-1}?

ITQ 2 Why do you stop the watch on the thirty-first pulse?

EXPERIMENT CONTINUED

EXPERIMENTAL PROCEDURE

First you need to draw up a Table in your Notebook to record your results.

Sit quietly for five minutes. Now take three measurements of pulse rate while still at rest and record each measurement in your Table.

Convert your results to beats per minute and calculate the average resting heart rate. Enter this result in your Table.

Now take the exercise. Climb onto and off a step the size of a normal staircase step around 100 times. You might have to adjust the speed of exercise or the number of steps to suit your own fitness. The aim of the experiment is not to produce exhaustion, but a fit person might not find 100 steps sufficient exercise to make a substantial change in their heart rate. *Only do what you know is safe and suitable for you or your subject.*

Immediately exercise is complete, measure and record the pulse rate. Take a further measurement of pulse rate starting 2 minutes after the end of the exercise period. Take a third measurement at 5 minutes, and a fourth at 10 minutes. You will only be able to measure each of these pulse rates once. Enter these results in your Table.

You have now completed the experiment, but remember to check that you have all the details you need to answer any associated assignment questions.

You should have found that exercise increases heart rate, and that the heart rate does not slow down as soon as the exercise stops. Assuming relative fitness, then the resting pulse rate will probably fall in the range of around 50–75 beats per minute, and your first reading after exercise stops is likely to be around 120–180 beats per minute. This is the usual range for most people: others—who are nonetheless entirely healthy—may have values of less than 120 or more than 180 beats per minute.

Now this increased rate means that the amount of blood being pumped by the heart (the cardiac output, you remember) has increased during exercise. In fact the increase would have been from around 5.5 litres min^{-1} to 25 litres min^{-1} during heavy exercise. This increase is due not only to the increase in *rate*, but also to an increase in **stroke volume**—that is, the volume of blood pumped out by the heart during a contraction: around 80 cm^3 at rest, rising to 140 cm^3 during exercise. There is a simple relationship between cardiac output, stroke volume and heart rate:

$$\text{cardiac output} = \text{stroke volume} \times \text{heart rate} \qquad (2)$$

As an example, take the figure of 70 beats min^{-1} at rest, and the stroke volume of 80 cm^3:

$$\text{cardiac output} = 80\,cm^3 \times 70\,\text{beats}\,min^{-1} = 5\,600\,cm^3\,min^{-1}$$

$$= 5.6\,\text{litres}\,min^{-1}\,(\text{because 1 litre} = 1\,000\,cm^3)$$

ITQ 3 During heavy exercise, the heart rate of an athlete was measured as 170 beats min^{-1}. If the athlete's cardiac output was 25 litres min^{-1}, what was the stroke volume of the heart (in cm^3)?

Having measured heart rate yourself, you may be wondering how figures for cardiac output can be measured in a human without major surgery. They can, in fact, be measured by a fairly simple procedure that depends on injecting a dye into a vein, followed by the collection of a number of blood samples. The method, used regularly to investigate certain heart defects, is included here to illustrate how internal physiological data can be found in living subjects.

STROKE VOLUME

COLORIMETER

By determining how fast the injected dye is circulated and then by how much it is diluted, cardiac output can be calculated. Look at Figure 12a to see what is going on. 5 milligrams of blue dye is injected into a vein at point I. From this point it travels to the heart, on through the lungs, back to the heart and out into the arteries. The amount of dye in the blood is sampled by drawing off a series of samples through a cannula (a sort of tap pushed into an artery) at point S. Dye concentration is measured in a machine termed a **colorimeter**: a beam of light passes through the sample and the amount of light transmitted is related to the concentration of the dye. If the concentration of the dye in each sample is plotted against time for a person who exercises continuously throughout the test, the red curve in Figure 12b is obtained. A resting subject produces a curve of the type shown by the black line.

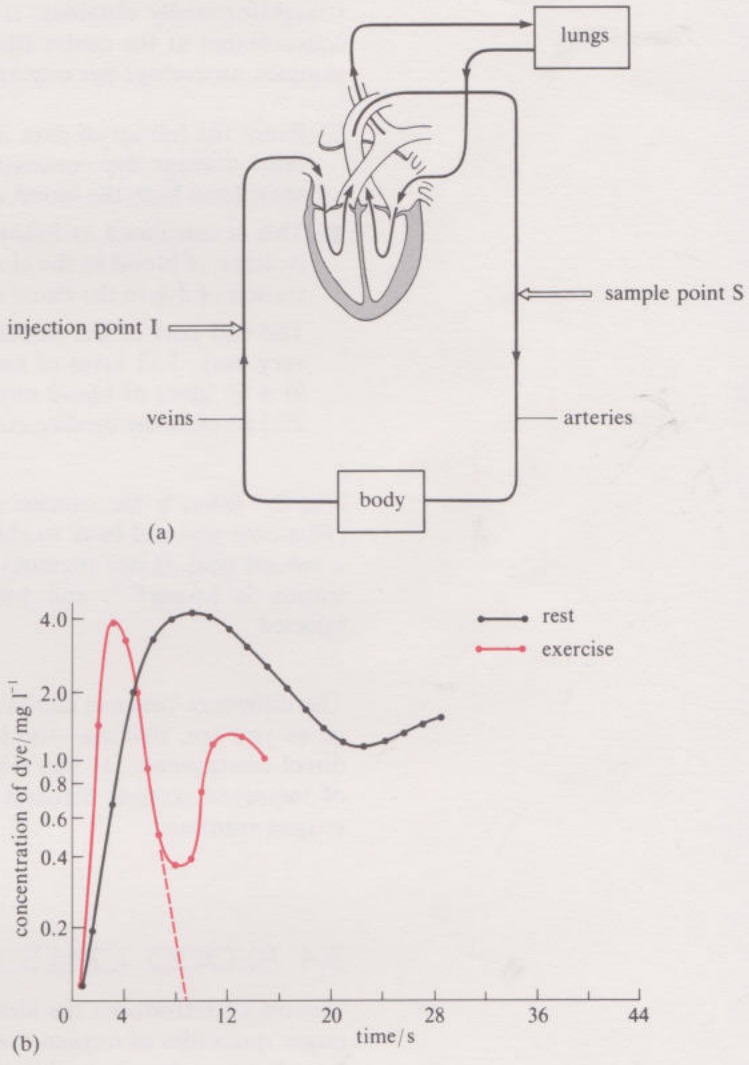


FIGURE 12 Measurement of cardiac output in a human. (a) Injection of dye into bloodstream at point I and sampling at point S: arrows show the route taken by the dye. (b) Dye concentration in blood samples from a person at rest (black line) and exercising (red line).

ITQ 4 Imagine a local 'cloud of blue dye' in the blood near point I and picture what happens as that blood moves through the blood vessels towards point S.

(a) Why does the dye level rise, fall and then rise again?

(b) Why does the peak in the exercise curve occur earlier than in the rest curve?

With the answer to this ITQ in mind, how can we calculate (from the results in Figure 12b) how fast the dye is circulated? You can determine this directly for the exercise curve, by measuring the time taken for the cloud of dye to travel from S, right round the system and back to S again. As you

PLATELETS
WHITE CELLS
RED CELLS
GLOBIN
HAEM

see, it is 9 seconds—the distance between the two peaks. In fact, it is usually more convenient to measure the time from 'no dye at all' (the origin of the graph) to 'no dye at all, again'. You have to find the latter by extending the downwards part of the first peak to the baseline.

□ The exercise curve has been extended for you (shown as a dashed line in Figure 12b). At what time does it cross the baseline? What conclusions do you draw?

■ It crosses after 9 seconds. This is the same as the time between the two peaks.

So the cloud of dye in the blood circulates in 9 seconds—but how much blood is there in that cloud of dye? As noted earlier, we can find this by seeing how much blood must have been involved in diluting the injected dye (5 mg of it, remember) to the concentration of it in the cloud. The latter value is not straightforwardly obtained: it is very dilute at the edges of the cloud and concentrated at the centre (the curve's peak). By combining data from 30 samples, an average dye concentration can be calculated.

□ From the full set of data for the 30 samples (not given here), the calculated average dye concentration is $1.5\,mg\,l^{-1}$. 5 mg was injected. What must have been the blood volume in the dye cloud?

■ This is calculated as follows: 5 mg (mass of dye injected) divided by V (volume of blood in the cloud of dye) equals $1.5\,mg\,l^{-1}$ (average concentration of dye in the cloud of dye). Hence, $V \approx 3.33$ litres.

The end part of the calculations associated with the procedure is now very easy. 3.33 litres of blood circulated in 9 seconds. Therefore (3.33/9) × 60 litres of blood circulated in one minute. The calculated result, 22.2 litres, is the cardiac output.

ITQ 5 What is the cardiac output for the resting curve in Figure 12b? (This time you will have to extend the line to determine circulation time, as a second peak is not present.) You are given that the average dye concentration is $1.6\,mg\,l^{-1}$, and you should remember that 5 mg of dye were injected.

The difference between cardiac output in the resting and exercising subjects is, as you see, striking—the latter is nearly five times as great. This is a direct consequence (as you will see when we examine control mechanisms) of increased oxygen demand. Let us return, therefore, to the matter of oxygen transport.

3.4 BLOOD CELLS AND HAEMOGLOBIN

Section 3.1 introduced the idea that haemoglobin is able to transport much larger quantities of oxygen than would be possible in merely physical solution. But how does it do this, and where is the haemoglobin in blood?

In the discussion of heart function, blood was treated as if it were just a liquid. It is, however, more complex than that. Blood contains cells and cell fragments of several types (Plate 10). **Platelets** are part of the clotting mechanism that seals wounds, and not only the wounds that we are aware of. They plug small holes that continuously appear in the walls of blood capillaries, for example. **White cells** have several functions concerned with protection against infection. **Red cells** are the most numerous type of blood cell, and their principal function is to transport oxygen and carbon dioxide. It is these that contain the haemoglobin molecules. Unlike white cells, both platelets and the red cells of mammals have no nuclei. The liquid component of blood is called the plasma. It is an aqueous solution of inorganic salts, containing proteins that, among other functions, help to maintain the water balance between cells and blood.

As you see from Plate 10, the human red cell has the shape of a biconcave disc. The cell membrane is very elastic, and the cells can undergo considerable deformation without damage. This is a necessary property for cells that are going to be forced through very narrow diameter tubes. The shape of the cell aids its role as a transport agent for gases. The average diameter is 7 μm, and the surface area is 140 μm^2. If the contents of the cell were contained in a sphere, the surface area would be smaller—thus, the biconcave shape provides a much greater area over which gas diffusion can take place. Both of these features—elasticity and shape—are further examples of the relationship of structure to function at the physiological level.

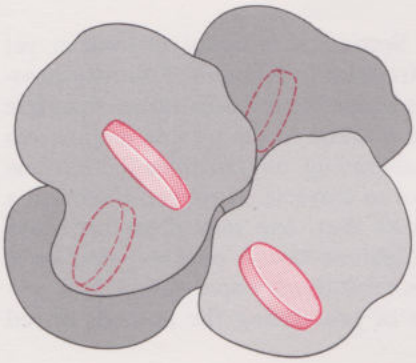


FIGURE 13 The structure of haemoglobin A, showing the four polypeptide chains constituting globin, and the four associated haem groups. This is a simplification of the model shown in Plate 2 of Unit 22.

Haemoglobin within red blood cells is able to combine with and thus transport both oxygen and carbon dioxide. The latter will be discussed again in Section 4, when the removal of metabolic products is discussed. For now let us focus on oxygen transport. Look at Figure 13. This is a simplified drawing of the haemoglobin structure that you met in Unit 22 (Plate 2). The rather large molecule (its relative molecular mass is about 66 000) consists, you may remember, of four polypeptide chains. This constitutes the **globin** part of the molecule. Attached to each of these is a **haem** group. The whole molecule is usually written as Hb. (Note that Hb is *not* an element but is a generally accepted abbreviation for haemoglobin.) These haem groups are shown in red in the Figure. Each haem group, which consists of a nitrogen-containing ring structure in the centre of which is an atom of iron(II), is able to bind one oxygen molecule. Overall, therefore, one haemoglobin molecule is able to bind, in a fully *reversible* way, four oxygen molecules thus:

$$\underset{\text{haemoglobin}}{Hb} + 4O_2 \rightleftharpoons \underset{\text{oxyhaemoglobin}}{HbO_8} \qquad (3)$$

Note that the iron remains as iron(II) when this oxygen binding reaction occurs.* Haemoglobin containing oxidized iron (iron(III)) is abnormal and is biologically inactive; in fact, red cells contain enzymes whose specific function it is to ensure that the haemoglobin iron remains as iron(II). It is this reaction that gives blood the tremendously large oxygen-carrying power mentioned in Section 3.1: plasma alone can carry only 5 cm^3 per litre compared with 200 cm^3 per litre of whole blood. Table 3 lists the latter along with other characteristics of blood.

TABLE 3 Some characteristics of human blood. Values are averages for an adult male: there is variation between individuals

number of red cells	$5.5 \times 10^{12}\,l^{-1}$
haemoglobin content	$155\,g\,l^{-1}$
oxygen carrying capacity	$200\,cm^3\,l^{-1}$
typical oxygen content of arterial blood	$195\,cm^3\,l^{-1}$
typical oxygen content of venous blood	$150\,cm^3\,l^{-1}$
plasma pH of arterial blood	7.40
plasma pH of venous blood	7.37

When arterial blood reaches the tissues, it gives up oxygen (Equation 3). It does this *because* oxygen concentration in the extracellular fluid is low as a direct consequence of mitochondrial activity in adjacent cells. Diffusion of oxygen along a concentration gradient—exactly the story you are familiar with from Section 2—now occurs.

Table 3 contains a further important and intriguing item of data. Look at the values for oxygen in arterial blood and oxygen in venous blood.

☐ Compare these values. What can you conclude?

■ Only part of the oxygen carried in the arteries of the systemic circulation is given up when it reaches the tissues.

* This contrasts with the situation with the cytochromes described in Unit 22. There, the reduced forms contained iron(II) and the oxidized forms iron(III).

VISCOSITY

CARBONIC ANHYDRASE

Although venous blood contains *less* oxygen than arterial blood ($150\,cm^3\,l^{-1}$ compared with $195\,cm^3\,l^{-1}$), it still contains a good deal. This means that in most tissues of the body arterial blood gives up only about a quarter of its total oxygen content in the tissue, leaving a large reserve that can be called upon in times of strenuous exercise.

☐ In Section 3.3 you came across two other ways in which the circulatory system can respond to the demands of exercise. What were they?

■ Heart rate and stroke volume can increase. The ability to yield up extra oxygen, referred to above, is a third response.

As we draw towards the close of this Section, it is useful to look at yet another example of the adaptation of structure to function. You may possibly have wondered why haemoglobin is inside the red cells rather than free in plasma solution. At first sight, simple solution in the plasma might seem advantageous in terms of 'loading and unloading' oxygen since there is one membrane less for the oxygen molecules to traverse. However, there are a number of physical and chemical factors that, one may speculate, have perhaps favoured the evolution of 'membrane-bound packets'—red cells, that is. On somewhat safer ground than evolutionary speculation, it is certainly possible to list the *consequences* of postulating the absence of red cells.

(a) The **viscosity** of the blood would be very much higher if the haemoglobin were free in the plasma. Viscosity is a measure of the resistance to flow of a liquid. Upset a cup of tea, and the tea appears to flow all over the place almost instantly. However, knock over a cup of treacle and you should be able to pick it up again long before all the treacle has flowed out. At room temperature, treacle has a much higher viscosity than tea. Increased viscosity in the plasma would offer a greater resistance to flow and so require a much stronger pump.

(b) A number of red cell enzymes catalyse reactions involving haemoglobin: an example mentioned earlier is that involved in keeping iron in its iron(II) form. It is difficult to see how these could interact effectively with haemoglobin molecules if the latter were not confined within the cell membrane.

(c) A number of molecules synthesized within the red cell alter the affinity of haemoglobin for oxygen, and are significantly involved with regulating the release of oxygen. Though such detail cannot be discussed here, these systems, also, could not readily function in a cell-less system.

This concludes our review of circulation in relation to oxygen transport. Oxygen is, of course, just one component of the oxidative equation we have chosen to guide our discussion of physiology. Logic, in the sense of dealing with the *reactants* of Equation 1 (Section 2) might seem to suggest that glucose provision should be our next concern. In fact, as the generation of CO_2 is so closely related to the consumption of oxygen, it is to that side of the equation we turn in Section 4.

SUMMARY OF SECTION 3

1 The circulatory system in mammals has functions including the supply of oxygen and oxidizable substances to cells, and the removal of metabolic products and of heat.

2 The heart provides a double circulation. The pulmonary circulation and systemic circulation are separately pumped by the heart.

3 The cardiac output alters with demand. Both heart rate and stroke volume can vary.

4 Cardiac output can be measured by injecting dye and following the progressive dilution of the dye during each circuit of the blood system.

5 Blood consists of plasma, platelets, white cells and red cells. The red cells contain haemoglobin, which has the ability to combine *reversibly* with

oxygen (and carbon dioxide) at the lungs and again at the capillaries in the tissues.

6 The presence of red cells alters the viscosity of the blood. Haemoglobin is confined within the cells, and this reduces viscosity.

7 The physiology of the circulatory system provides many examples of the close relationship of structure to function.

8 Such structure–function relationships are accounted for in terms of the theory of evolution by natural selection. Teleological statements ascribing purpose are to be avoided.

SAQ 3 Which two of the following statements about the mammalian heart and circulatory system are true?

(a) All arteries carry oxygen-rich blood.
(b) Most veins carry oxygen-depleted blood.
(c) All the blood passes through the lungs, but not all passes through the heart.
(d) In the heart the blood passes from the atria into the ventricles, but the chambers on each side are separated so there are two independent flow routes taken by the blood.

SAQ 4 In the experiment, you should have found that the heart rate did not immediately return to the resting level after the exercise stopped. Suggest a possible biochemical reason for this.

SAQ 5 Why is it advantageous that blood should have low viscosity?

4 REMOVING THE PRODUCTS OF METABOLISM

There remains from Equation 1 (Section 2) the question of what happens to carbon dioxide and water. Also, from Unit 22, Section 7, which dealt with other fuels than glucose, you should recall that there will be waste nitrogen compounds to dispose of. Finally, associated with ATP production and usage there will be metabolic heat to be dissipated. This Section considers the ways in which organisms remove the products of metabolism.

4.1 DISPOSAL OF CARBON DIOXIDE

Virtually all the carbon dioxide produced as the result of metabolism diffuses directly into the bloodstream. Therefore, the blood transports it to the lungs, into which it is released by diffusion and from which it is discharged in exhaled breath.

In Unit 22 you were shown the precise relationship between the amount of oxygen used during catabolism, and the amount of carbon dioxide formed. Carbon dioxide reacts with water, as shown in Equation 4:

$$CO_2 + H_2O \rightleftharpoons H^+ + \underset{\text{bicarbonate ion}}{HCO_3^-} \qquad (4)$$

Most of the CO_2 produced in the tissues during catabolism is transported to the lungs in the form of bicarbonate ions. In the red cells the enzyme **carbonic anhydrase** catalyses the formation of H^+ and HCO_3^- from H_2O and CO_2. So the reaction goes much faster in the red cells than in the plasma, where there is no carbonic anhydrase. The two ions produced are quickly removed from solution in the cells since the H^+ is taken up by the haemoglobin, and the HCO_3^- diffuses back into the blood plasma where its concentration is lower.

UREA

☐ How do you think it is possible for haemoglobin to take up H^+ ions?

■ As with many proteins, there are many *R groups* along the polypeptide chain that, being ionized, can take up hydrogen ions.

This continuing process of bicarbonate formation followed by its diffusion into plasma maintains a CO_2 concentration gradient between the respiring tissues (high CO_2 concentration) and the red cells (low CO_2 concentration due to bicarbonate formation). Study Figure 14, which summarizes this sequence of reactions. At the lungs, the hydrogen ions taken up by the haemoglobin during the passage of the blood through the tissues are released again. These react with the bicarbonate ions of the plasma to give water and CO_2.

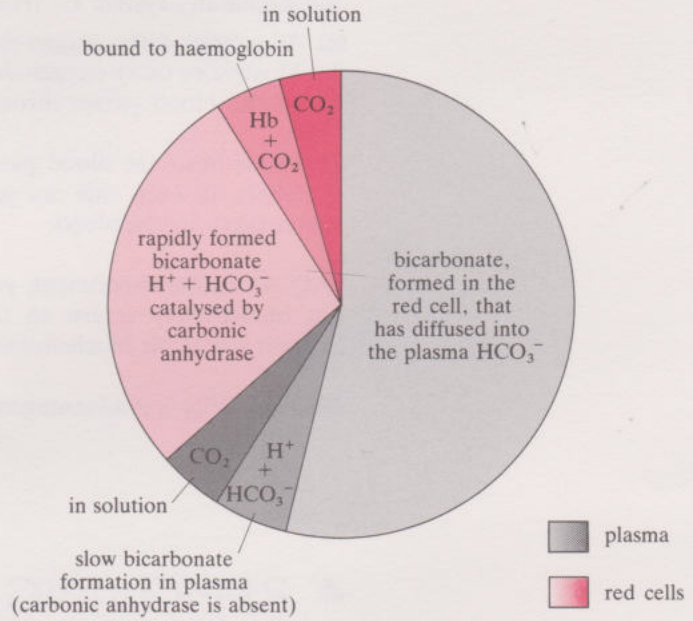


FIGURE 14 The removal of carbon dioxide from tissues by the formation of HCO_3^- in the red cells, which then passes into the plasma. The pie diagram shows the percentage of carbon dioxide in each of the different categories: for example, about 70% of carbon dioxide is in the plasma.

☐ How do you think the CO_2 leaves the capillaries of the alveoli?

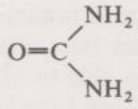
■ By diffusion along a concentration gradient: once free as a gas in the alveolar spaces, it is breathed out during exhalation.

This sequence of reactions is important because, by forming HCO_3^-, carbon dioxide can be carried in the blood. The acidification of the blood resulting from this dissociation, which alters its pH (Table 3, Section 3.4), forms the basis of the mechanism used by the body to detect increased tissue respiration and hence the need for an increase in breathing rate. We shall be considering the control of breathing rate further in Section 6.

4.2 ELIMINATION OF WATER AND NITROGEN COMPOUNDS

As CO_2 is blown out of the lungs to get rid of it, so some water is also lost by evaporation from the alveolar surface. However, this route only accounts for about 2% of the total water loss in a person at rest at 20 °C; most is lost by other ways.

ITQ 6 From general knowledge, list routes by which the human body loses water.


urea

One of the routes by which water is lost is via the bladder. The main nitrogen-containing compound of human* urine is **urea**, an organic compound whose molecular structure is shown in the margin. Water is also lost in other ways, for example by sweating (see Section 6) and, indeed, by breathing, in which water evaporates from the surface of the alveoli.

Where does the nitrogen in urine come from?

One source is the catabolism of amino acids: the NH_2 group is split off each amino acid molecule and then converted (by another metabolic pathway) to urea. You have met deamination (removing amino groups from amino acids) in Unit 22, Section 7. The non-nitrogen parts that are left, you may remember, are dealt with by the central pathways—giving CO_2, H_2O, ATP and heat in the usual way.

Waste nitrogen compounds must be removed, as in high concentrations they are damaging. However, as urea has to be disposed of in solution, an inevitable consequence is that water is lost from the body. The kidneys remove urea from the bloodstream, where it has a concentration of about $300\,mg\,l^{-1}$, and forms a more concentrated fluid (urine) for disposal. The urea concentration in urine can be as high as $20\,g\,l^{-1}$.

We have now looked at the supply of oxygen and, though only briefly, the disposal of wastes: CO_2, water, and nitrogen compounds. These are all the major products of catabolism except one—heat.

4.3 HEAT TRANSFER

All organisms produce heat as a consequence of their metabolic activity. You know from Unit 22, Section 6.1, that—except when doing external work (the transfer of gravitational or kinetic energy in lifting or throwing, for example)—*all* the energy released in catabolism ultimately appears as heat. Thus, if you eat food that yields 10 000 kJ on oxidation, all of it (apart from any expended on external objects) will ultimately appear as metabolic heat. It is this, in terms of Equation 1, that seems at first sight to be an unwanted product. In fact, however, the term 'waste' is not wholly appropriate when applied to heat. It is plain from general knowledge of the world around us, that heat is important to all organisms—in the sense that retained heat increases body temperature and heat disposal reduces body temperature.

□ Why, in all groups of organisms, is it important that internal temperature should neither be too low nor too high?

■ The rate of any chemical reaction increases with temperature. At temperatures lower than normal (for a particular organism), biochemical reactions, hence bodily activities, would occur at a lower than normal rate. If body temperature is too high, proteins become denatured (Unit 22, Section 4.3), leading ultimately to death.

In some animals (those described as 'cold-blooded' in everyday language), heat production through their own, rather slow, metabolic processes is often inadequate for their temperature needs. Such organisms—lizards, for example—frequently *take in* heat by moving into a warm part of the environment, moving out of it when they are warm enough: a simple but often very effective kind of control. It is also plain that for organisms of this type, 'getting rid of metabolic heat' is no problem at all: metabolic rate is so low, in comparative terms.

* In other taxonomic groups the principle nitrogen compound excreted may be other than urea. For example, it is ammonia (NH_3) in fish and uric acid (a more complex organic nitrogen molecule) in birds and reptiles. Uric acid is rather insoluble and is the white powdery constituent of bird lime.

HYPOGLYCAEMIA

HEPATIC PORTAL VEIN

Birds and mammals are the two groups of organisms that maintain a constant inner temperature. As we shall see later, the regulatory systems that have evolved are quite complex—being able to maintain temperature constancy in the core of the body *either* when heat loss is high and heat production is low (when asleep in cold weather, for example) *or* when heat loss is low and heat production is high (when running in hot sun, for example). Sometimes, therefore, heat must be produced and conserved; on other occasions, it must be disposed of to the environment.

Section 6 considers, in some detail, how the balance between 'heat in' and 'heat out' is achieved. The point of importance at present is that blood has a crucial role in the transfer of heat from the tissues in which it is catabolically generated via the detectors of temperature that form part of the control system, to the skin from which heat is lost to the environment.

SUMMARY OF SECTION 4

1 Carbon dioxide is produced in the cells as a result of metabolism, and is transported to the lungs in the bloodstream.

2 Very little CO_2 can be carried in solution in the blood plasma, but the enzyme carbonic anhydrase in the red cells catalyses the formation of bicarbonate, which increases the carrying capacity of the blood.

3 Bicarbonate is reconverted to CO_2 in the lung capillaries and passes to the alveoli by diffusion.

4 In humans (and in some other organisms) waste nitrogen is removed, in solution, in the form of urea by the kidneys. This results in a water loss since the concentration of urea in the urine is limited.

5 Water is lost through urine production, sweating and evaporation of alveolar water.

6 Blood has an important role in transporting metabolic heat and is an important part of systems that some animals employ in maintaining a constant body temperature.

5 SUPPLY OF GLUCOSE

As you saw in Unit 22, Section 6, glucose is a major source of energy in the cell. It has special significance because certain areas such as the brain are particularly sensitive to a reduced supply of glucose. The brain cells need glucose as a substrate for metabolism, yet do not themselves store glycogen.

What is the significance of the lack of glycogen stores in the brain cells?

Glucose is converted to glycogen in most tissues, notably liver and muscle. Glycogen, you will remember, is a long chain polymer of glucose, and it is relatively insoluble in blood. The glycogen acts as a glucose store—the muscles of an adult human male may contain up to 150 g of glycogen, and the liver 60 g. As no glycogen is stored by the brain cells, they are *totally dependent on the direct supply of glucose from the blood.* In this Section you will see how the level of glucose circulating in the blood is regulated, and you will discover some of the consequences of impaired regulation in humans.

5.1 REGULATION OF BLOOD GLUCOSE LEVELS

The level of glucose in the blood is relatively easy to measure, as you will see in the TV programme associated with this Unit. The normal level of blood glucose in humans before breakfast is 4.5–5.5 mmol l^{-1} (810–990 mg l^{-1}). After a meal that contains carbohydrates (for example, cornflakes with milk and sugar) the level will rise temporarily to around 7 mmol l^{-1}. Going without food for 24 hours will cause the level to fall to a value close to 3.5 mmol l^{-1}, but the value will not fall further even if fasting is prolonged. This is principally to protect the brain cells, because **hypoglycaemia** (low glucose level) is rapidly damaging.

As Figure 15 shows, the level of glucose measured in the blood is largely the balance of inflow from the intestine against outflow into the cells. Glucose, fructose and other sugars are the final products of the digestion of carbohydrates in the intestine. These diffuse out of the intestine into the capillaries that run through the intestinal wall and are carried into the **hepatic portal vein**. This vein takes blood to the liver direct from the intestine. In the liver, fructose and other sugars are converted to glucose which is either stored as glycogen or liberated into the bloodstream.

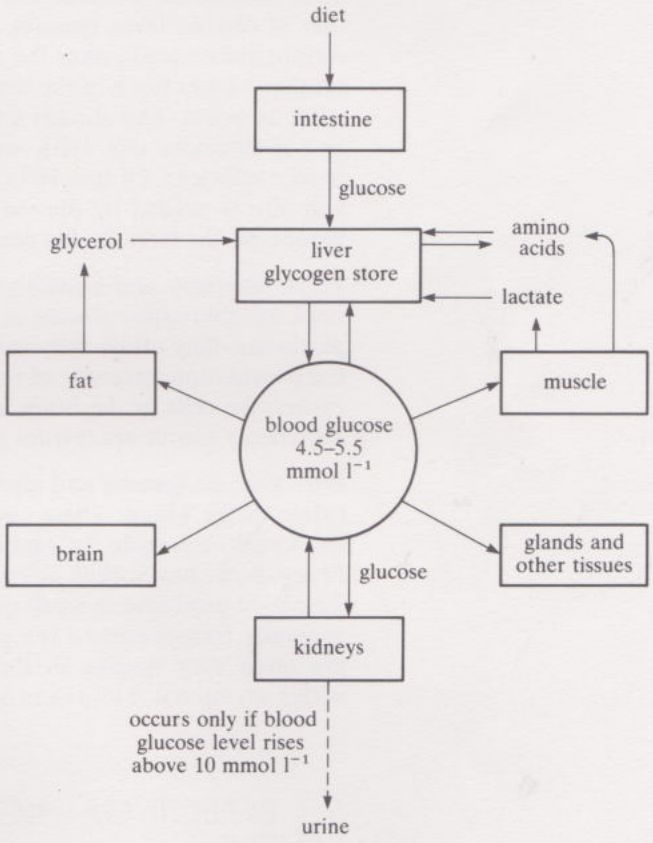


FIGURE 15 The regulation of blood glucose by the liver. There is almost total reabsorption of glucose from the urine within the kidney, to minimize loss. Only if the blood glucose level gets very high is a significant amount of glucose lost in the urine.

It is the liver that plays the key role in adjusting the level of blood glucose and thus regulating supply to match demand. This role is summarized in Figure 15, and is also considered in the TV programme, when the results from blood glucose measurements are discussed.

GLYCOGENOLYSIS

GLUCONEOGENESIS

HORMONE

TARGET TISSUE

HYPERGLYCAEMIA

GLUCAGON

ADRENALIN

INSULIN

DIABETES

5.2 RESPONSES TO LOW BLOOD GLUCOSE LEVELS

There are several ways in which the body responds to low levels of blood glucose. The obvious first response is the feeling of hunger that is generated. Eating is a fast way to raise blood glucose levels. The other major responses are **glycogenolysis** and **gluconeogenesis**.

Glycogenolysis is the breakdown of glycogen to glucose, and it occurs in the liver within minutes of the blood glucose level falling to a dangerous level. The adult human liver, you remember, normally contains about 60 g of glycogen, and, if all this were metabolized, around 1 000 kJ of energy would be provided. Though this is not a lot by comparison with the total daily requirement of energy, it does give a short-term protection to the brain and other tissues without glycogen stores. For comparison, a typical daily requirement for an adult human male of 40–50 years of age weighing 65 kg is 12 600 kJ day^{-1}.

Glycogenolysis provides a short-term protective response, by providing glucose from glycogen. In contrast, gluconeogenesis provides a less rapid but longer-term solution. The term means the new ('neo') synthesis ('genesis') of glucose ('gluco'). Thus it involves the synthesis of glucose from other molecules. Glucose can be synthesized in the body from (a) lactate that is derived from muscles, (b) glycerol from the breakdown of fats, (c) certain amino acids, after the amino group has been removed. Most of this synthesis takes place in the liver, and about 180 g of glucose can be produced in 24 hours. This sounds a good deal, but if there were no food available and if therefore this 180 g were the *only* source of glucose, it would be barely sufficient. Of this 180 g, the brain and nervous system require 140 g, and 30 g is needed by the red cells—not leaving much at all for the other tissues, particularly the big consumers like muscle.

Thus, muscles—and remember that the heart is almost entirely muscle—need an alternative source of energy when glucose is in short supply. In particular, they utilize fatty acids that yield much ATP when catabolized by the β-oxidation pathway of the muscle mitochondria. In contrast, as noted earlier, the cells in the brain and nervous system are unable to metabolize *any* energy source apart from glucose.

Both gluconeogenesis and glycogenolysis are initiated by chemicals that circulate in the blood. These chemical messengers are called **hormones** (from the Greek *hormaein*, 'to excite'). More is said about these in Section 5.4. Many processes within animals and plants are controlled by hormones. These are produced in small quantities, often in certain special cells, and are generally transported to the place where they have their effect. Hormones are often very specific in their action, affecting only a particular tissue within an animal. This tissue is called the **target tissue** for that hormone.

5.3 EFFECT OF HIGH BLOOD GLUCOSE LEVELS

Hyperglycaemia, raised blood glucose level, is not of itself harmful—but the consequences may be if the effect is prolonged. In people with diabetes, the resting blood glucose level may be as high as 11 mmol l^{-1}, rising to 22–28 mmol l^{-1} after a meal, compared with the normal figures of 4.5–5.5 mmol l^{-1} at rest and 7 mmol l^{-1} after a meal. A consequence of hyperglycaemia (above 10 mmol l^{-1}) is that the kidney no longer reabsorbs all glucose and thus glucose appears in the urine. As in the case of urea, glucose has to be disposed of in solution. The glucose loss increases the amount of water lost, and so dehydration of the body may result. Dehydration produces thirst, and an increase in water intake. Important ions such as sodium and chloride are washed out with the glucose in the urine. Excessive loss of ions and water can lead to coma and death.

Thus hyperglycaemia has adverse effects and, as you saw earlier, hypoglycaemia is equally to be avoided. How, then, is the level to be maintained within narrow limits?

5.4 HORMONES AND THE REGULATION OF BLOOD GLUCOSE LEVELS

A detailed answer to this question must be postponed until Section 6, where regulatory systems are considered in some detail. However, it is useful to remind ourselves here that glucose levels are markedly affected—in one direction or the other—by several different kinds of hormone that are secreted into the blood. These—acting on glycolysis, gluconeogenesis, the uptake of glucose by cells, and on still other processes—have a powerful effect on blood glucose level. The three principal hormones involved in the regulation of blood glucose levels in humans are as follows.

1 **Glucagon** causes glycogenolysis in the liver, and increases the rate of gluconeogenesis. Because it raises blood glucose level, it is said to have a *hyperglycaemic effect*.

2 **Adrenalin** promotes glycogenolysis in liver and muscle and, therefore, is also hyperglycaemic. In muscle it has the effect of increasing lactate production, and lactate is a substrate for gluconeogenesis in both liver and muscle. A fall in blood glucose level produces an increased level of adrenalin in the blood. Adrenalin also inhibits the action of the third principal hormone, insulin.

3 **Insulin** has a number of effects, all of which tend to *lower* the blood glucose level: in fact, it is the only *hypo*glycaemic hormone. Its main effect is to promote the transfer of glucose out of the blood and into cells. One of the ways that this comes about is that insulin enhances the activity of some of the enzymes involved in glycolysis. This increases the demand in the cells for glucose, and so reduces the blood glucose level.

Sufferers from **diabetes** have low levels of insulin in their blood, or insulin may be absent. As a result, their blood glucose levels will be high, but the level of glucose in the cells will be low. Diabetes is treated by controlling the diet and, often, by injecting insulin. Injections have to be repeated daily, since insulin is rapidly degraded in the body—half of it being destroyed within about 10–15 minutes. As you should remember from Unit 22, Section 3.4, insulin is a protein that is destroyed by proteolytic (protein-destroying) enzymes, so it cannot be taken by mouth because it would be broken down by enzymes in the intestine before it could diffuse through into the bloodstream. Injections of insulin cannot produce a perfect match between blood glucose levels and blood insulin levels. Thus, even though insulin treatment is very effective, it is still possible for the blood glucose level to rise or fall too much. As a result diabetics need to monitor their blood glucose levels regularly. One method available to them is to use colour-indicating strips of the type shown in use in the TV programme. The strips are sensitive to glucose in a blood droplet, and change colour. The colour gives an accurate measure of glucose concentration, which can be read directly using a cheap test instrument (also shown in the TV programme).

Hyperglycaemia can be recognized by an increased feeling of thirst. Hypoglycaemia can be recognized because the adrenalin level in the blood rises, and adrenalin has a number of other recognizable effects on the body, producing nervousness, weakness, anxiety, increased heart rate, and headache.

SUMMARY OF SECTION 5

1 The bloodstream provides glucose as a metabolic substrate for cells.

2 Cells in the brain and nervous system can utilize only glucose as a source of energy. For them, low blood glucose levels are harmful.

3 A number of mechanisms are utilized to maintain blood glucose at a safe level, even during starvation. Glycogen stores are converted to glucose (glycogenolysis), and glucose is synthesized from a variety of substrates (gluconeogenesis). These changes occur mainly in the liver. Muscles catabolize fats, thus sparing glucose for brain tissue.

HOMEOSTASIS

REFERENCE LEVEL

RECEPTOR

SIGNAL

MONITOR

EFFECTOR

NEGATIVE FEEDBACK

POSITIVE FEEDBACK

4 A hormone is a molecule that is synthesized by one group of cells and exerts its effect upon another group—its target cells.

5 Some hormones initiate glucose synthesis and glycogen breakdown, thus raising blood glucose level. The two key hormones involved are glucagon and adrenalin.

6 In contrast, insulin is a hormone that lowers the blood glucose level by promoting metabolism in the cells.

SAQ 6 What would you expect to be the consequences of an injection of too much insulin into a diabetic person? How could the person cope with the consequences?

SAQ 7 What would have happened to the lactate levels produced in your blood after the stepping exercise? Think back to the experiment in Section 3.3.

6 CONTROL MECHANISMS

In the preceding Sections, you have seen how oxygen and glucose are supplied to cells, how water and waste compounds are removed, and how heat is transported. In each Section there has been a hint that all these processes are under some form of control. This is indeed the case and, because the principles of control are common to all biological systems, it is sensible to devote a separate section to the subject. As well as describing some of the common factors of control mechanisms, we look at a number of examples that bear upon the themes of this Unit.

The physiological control mechanisms in organisms keep order and prevent the onset of chaos. They maintain stability so that all the processes going on in the organism proceed at the optimum rate for the current circumstances. There is not just a single level of activity to be maintained, though. The blood flow required for a human at rest is different from the flow required by the same human swimming steadily across the Channel. The regulation of physiological function to maintain a particular stable state is called **homeostasis** (meaning 'staying the same').

> Can you think of an example (biological or otherwise) of a regulated process, and an example of an unregulated one?

There are many examples that you might have suggested of a regulated process, but a good one is the thermostatic control of heating systems in houses, or the cooling system in refrigerators, cars, etc. There are fewer common examples of unregulated processes. An explosion is perhaps the most familiar—you can't stop it or alter the rate once it has started!

In Figure 16, you can see how (at its simplest) a room thermostat controls a domestic heating system to produce a stable room temperature. This type of diagram is called a flow diagram, and similar ones are often used to describe the arrangement of physiological control systems. Many of the features of artificial systems, such as this central heating layout, are paralleled in biological regulation. It is instructive, therefore, to look for the *principles of regulation* in familiar manufactured systems and then to apply them to organisms. You should remember, however, that no analogy is quite perfect.

In the system in Figure 16, the aim of the control is to achieve a pre-set room temperature of 18 °C. Because it is pre-set, 18 °C is called the **reference level**. The thermostat senses the room temperature and, as it receives information about temperature, it can be termed a temperature **receptor**. When the temperature falls below the reference level, the receptor sends a **signal** to a control unit (the **monitor**), and that sends another signal to a pump and boiler (the **effector**) that circulates hot water through the radiator. As the radiators release heat into the room, the temperature increase

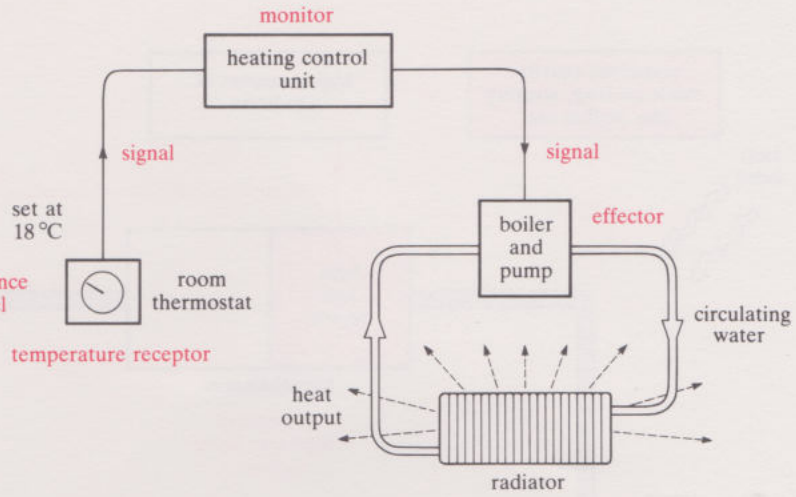


FIGURE 16 This is a simplified diagram of a central heating system (one room, one radiator). The terms in red are the functions of the various parts, and these terms can be applied unchanged to physiological systems. The reference level in this Figure is the temperature selected as a comfortable one by the occupant of the room: 18 °C.

is sensed by the thermostat. Via signals to the monitor and thence to the effector, heat production is switched off. Thus temperature is *controlled* at about the reference level.

A regulatory device in which a signal registering a temperature *increase* causes a change that *halts* (or *negates*) the temperature increase is said to depend on **negative feedback**—'feedback' because information is fed back to the effector; 'negative' because the activity of the effector is, when the reference point is reached, eliminated (negated) by the very effect it produces. In later parts of this Section, you will come across many examples of homeostasis—and *all* of them depend on negative feedback.

Positive feedback has no part—indeed, can have no part—in any homeostatic system. The following short discussion is included simply so that this potentially confusing term is made clear.

□ If *negative* feedback involves switching off an effector as a consequence of the change produced by the effector, what would *positive* feedback do?

■ The change produced by the effector would cause the effector to produce yet more change in the same direction. This is the very reverse of control—an explosion is a good non-biological example.

There are a few biological examples of positive feedback, all connected with processes that need to go rapidly and effectively to total completion. One such is the process of birth. The baby's head stretches the vagina as the contractions of the womb force it downwards. This distends the vagina, and the muscles respond to the stretching by *increasing* the number and strength of their contractions. This leads to more stretching, increased contraction, more push on the baby, and birth!

Let us return to negative feedback—as noted earlier, only this is involved in homeostatic systems. Six important terms have been introduced: receptor, signal, monitor, reference level, effector and negative feedback.

ITQ 7 Using only these six terms, complete the blanks in the following passage—in order to convince yourself that you understand their proper usage in the context of a control system.

In the heating system in Figure 16, a change in temperature is detected by the thermostat. The latter is termed the because it receives information about the temperature of the room. In this particular control system, the thermostat also contains the pre-set A passes from this point to the This compares the incoming information with its internal instructions and, as a consequence, sends a to the This is switched on, so heating the room. Eventually the

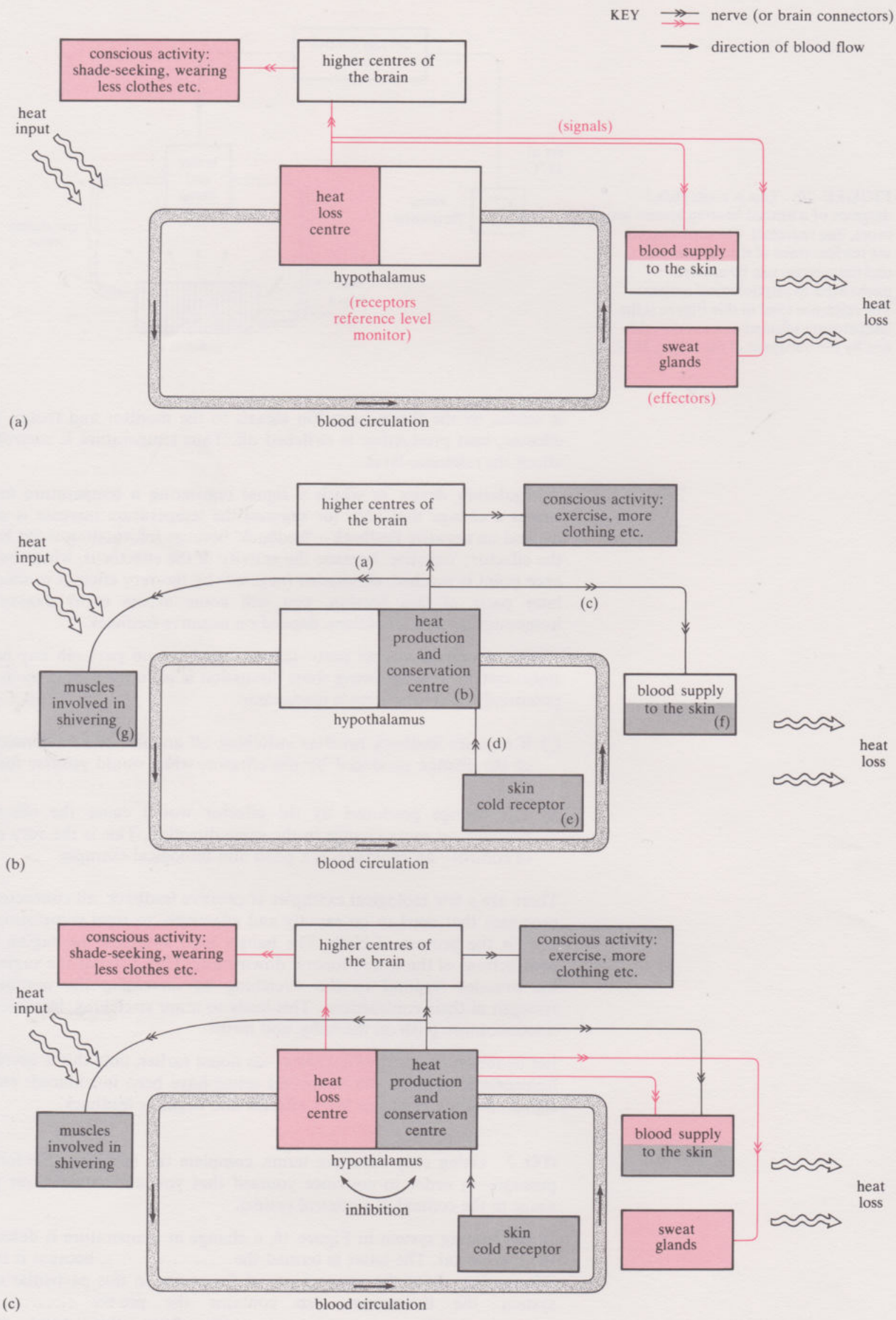


FIGURE 17 The thermoregulatory system in humans. (a) The cooling part of the system. Double arrows denote signals. (b) The heating and heat conservation part of the system. The bracketed letters refer to ITQ 8. (c) The two parts of the system combined. Note that when one centre in the hypothalamus is active, the other is inhibited, and vice versa.

HYPOTHALAMUS

temperature increases to the point at which the is exceeded. When this happens, the is switched off via the control system, so preventing any further rise. This is an example of feedback.

Let us turn to a biological control system and apply these terms. In Section 4.3 it was noted that, in birds and mammals, regulatory systems maintain the inner temperature very close to the reference level for each species—at around 37 °C in humans and many other mammals, a little higher for many birds. The thermoregulatory system is more complicated than the central heating system shown in Figure 16. This is because, depending on environmental conditions, the system has either to act as a *cooler* (keeping the temperature down) or as a *heating system* (keeping the temperature up).

Look at Figure 17. The first part of this, Figure 17a, is the cooling part, and it covers items that should be familiar to you from Section 4.3. The reference level is contained within the monitor—a small structure at the base of the brain called the **hypothalamus** (see Figure 18). The tissue of this organ is well supplied with blood from part of the systemic circulation, and has within it temperature receptors that measure blood temperature. When this rises above the reference level, impulses in nerves leaving the monitor send a signal to the effectors. These are the arterioles of the skin (dilation of them permits quantities of blood to travel near to the skin surface) and the sweat glands (production of sweat, which then evaporates, aids heat loss). Thus, through the activity of these effectors, heat is lost. The operation of negative feedback is plain to see—the nerve impulse signalling an increase in temperature brings about a change that *negates* that increase. Figure 17a shows the role played by each component. The *heat loss centre*, as this part of the hypothalamus is termed, also passes information about temperature to higher centres of the brain—and in turn initiates voluntary behaviour such as drinking, seeking shade, removing clothing and so on.

Now look at Figure 17b. This deals with the heat production and conservation part of the system. Once again, the hypothalamus contains the reference level and monitor—but this time a different part, called the *heat conservation and production centre*, is involved. The temperature of the blood entering this part of the hypothalamus may have some effect, but it is the cold temperature receptors in the skin that are of most significance. These send signals, via nerves, to the monitor where detected skin temperature is compared with the reference level. If the temperature is lower than this reference, nerve impulses signal the effectors to conserve heat (skin arterioles which contract, diminishing supply to the skin surface) and to generate heat (the muscles involved in shivering). Once again, information passed by the hypothalamus to the higher centres of the brain is very important, for certain voluntary activity such as vigorous exercise and putting on more clothing are more effective at maintaining body temperature than shivering.

Figure 17c shows the two subsystems combined—giving the overall, complex, system of thermoregulation. Try the following ITQ to check that you are familiar with the features of this kind of homeostatic system: you will meet others in later parts of this Unit and it is important to feel confident about the standard components.

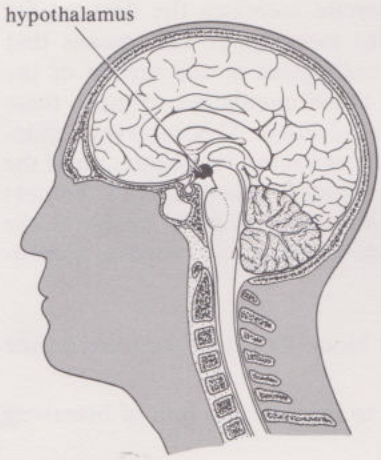


FIGURE 18 A human brain, showing the position of the hypothalamus.

ITQ 8 Assign one or more of the terms, *receptor*, *reference level*, *monitor*, *effector* and *signal* to the letters (a) to (g) in Figure 17b, so as to describe their role in this subsystem of the thermoregulation system in humans.

6.1 CONTROL OF BLOOD GLUCOSE LEVEL

The purpose of this brief Section is to link—in outline only—the general features of homeostasis that we have just discussed to the regulation of blood glucose. As you know from Section 5.4, the level of blood glucose is regulated through the action of the hormones insulin, glucagon and adrenalin. Thus, a significant difference between this regulatory system and that

PANCREAS

MEDULLA (OF BRAIN)

PONS

CEREBRAL CORTEX

CHEMORECEPTOR

CEREBROSPINAL FLUID

for temperature, is that the signalling is achieved through the circulation of *hormones* rather than by the transmission of *nerve impulses*. Otherwise, as you will shortly see, the system contains the familiar components of homeostasis and the expected operation of a negative feedback system. In the next paragraph we shall simplify the topic by considering only one hormone: insulin.

Insulin is, as has been said, the signal. It is secreted by particular cells (B cells) of an organ located near the liver called the **pancreas**, and, as you would expect, the amount of insulin secreted into blood passing through it is markedly altered by the level of glucose in that blood.

☐ Given (from Section 5.4) that insulin brings about a *fall* in blood glucose level, would you expect the pancreas to secrete more insulin or less insulin when blood glucose increases?

■ To achieve homeostasis, more insulin must be secreted when blood glucose is raised.

The pancreas contains the glucose receptors and the reference level. By responding to the detected glucose level, it also acts as the monitor. The effectors are all tissues in which the uptake of glucose is stimulated by the insulin, with liver tissue having a major role. This is, as you may have realized from earlier Sections, only part of the system. A further set of *hyperglycaemic hormones* (including glucagon and adrenalin) are involved in *raising* blood glucose when it falls below the reference level. However, in these much simplified terms, you should be able to see how blood glucose level is regulated by a system that depends on the negative feedback of information received in the pancreas, transmitted by a hormone and acted upon by tissues.

The importance and effectiveness of the system is brought out in the details of the TV programme. That programme also considers the role of breathing and heart rate in metabolism, and it is to the regulation of those features that we now turn.

6.2 CONTROL OF BREATHING

As you should have realized by now, exercise increases the demand for oxygen and, at the same time, it generates more CO_2. This means that there must be an increased exchange of both gases at the surface of the lungs and, also, an increase in the rate of blood circulation to move these gases from lungs to tissues and from tissues to lungs. This involves regulation of *breathing* and of *cardiac output*—and, of course, the regulation of the two must be closely linked. This Section considers breathing and the next (Section 6.3) deals with cardiac output. A feature of both stories is the detection and regulation of carbon dioxide in blood to preserve homeostasis.

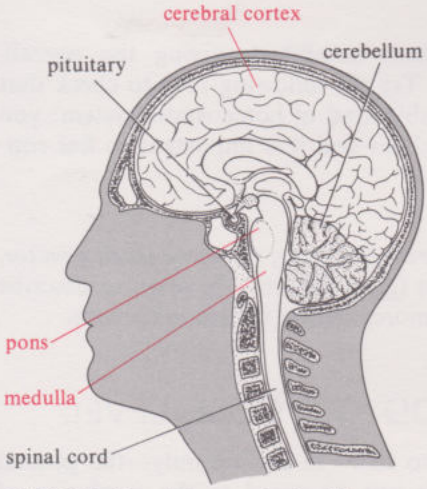


FIGURE 19 A human brain. The areas responsible for the control of breathing are lettered in red.

☐ What effect would you expect a raised blood CO_2 level to have on the rate of breathing and the heart rate?

■ You should expect a raised CO_2 level to increase the rate of breathing and to increase cardiac output.

☐ In theoretical terms, what alternative (or supplementary) method of control could also be effective?

■ Control could be achieved through blood oxygen levels. This time, a high level of blood oxygen should decrease breathing rate and decrease cardiac output.

Breathing in humans is a rhythmical process. An area of the brain called the **medulla** (Figure 19) contains a rhythm generator. This provides the basic pattern of breathing, and it runs continuously, providing a signal to

start inspiration (that is, breathing in). A second signal from a nearby part of the brain called the **pons** starts expiration (breathing out) by inhibiting the inspiration signal. The two form part of the 'Hering–Breuer reflex' (called after the two men who discovered it in 1868). As we shall see, variation in the relative timing of these two signals provides a means of control of breathing. Receptors in the lung walls detect how much the lungs have been inflated and, at a certain point, they trigger signals that stop the contraction of the respiratory muscles. This is another example of a feedback loop (involving, this time, signals in nerves and not via hormones).

But, how is the basic 'in-and-out' pattern of the Hering–Breuer reflex modulated, that is, how is it varied according to the needs of the body to obtain oxygen or eliminate CO_2? A limited amount of voluntary control is possible. People preparing to swim underwater can choose to breathe hard and so decrease the CO_2 level in their blood before starting—a process called hyperventilation. Similarly, once underwater the breath can be held at will for a short time. This voluntary control involves the higher centres of the brain in the **cerebral cortex**. But voluntary control is of relatively minor significance. More important is that the 'in-and-out' pattern adjusts automatically to achieve necessary gas exchange. The surfacing and now air-hungry diver does not have to *think* to breathe hard: he just does. How is this achieved?

In Equation 1 (Section 2) you saw that exercise uses oxygen and produces CO_2. In Equation 4 (Section 4.1) you saw that dissolved CO_2 leads to the production of H^+ ions and hence a decrease in pH. That decrease in pH is the basis on which receptors for carbon dioxide or **chemoreceptors** (so called because they respond to chemical signals) work. These receptors are located in the medulla of the brain (see Figures 19 and 20). Though the receptors are not in direct contact with blood, CO_2 diffuses from plasma into the fluid bathing the brain—the **cerebrospinal fluid**. Here H^+ ions are produced as described above. When the receptors detect an increase in H^+ concentration, a signal of nerve impulses reaches the effectors—in this case, the respiratory muscles—and an increased breathing rate results. Thus, *high* blood CO_2 levels produce an increase in the rate of breathing which results in a subsequent *lowering* of blood CO_2 levels. This is another example of negative feedback.

The system described above is complicated by a number of features. In particular, there is a further set of chemoreceptors, known as peripheral chemoreceptors, in the large arteries that carry oxygenated blood away from the heart (Figure 20). These differ from the receptors in the medulla in that they detect changes in *oxygen concentration* as well as in CO_2 concentration. For example, if the oxygen level falls, signals are sent to the brain which responds by increasing the rate of contraction of the respiratory muscles, and an increase in breathing rate occurs. In fact, these peripheral receptors are much more sensitive to changes in the level of CO_2 than to changes in the level of oxygen—and the oxygen level at the receptors would have to fall nearly to the level of oxygen in venous blood before they would initiate a signal.

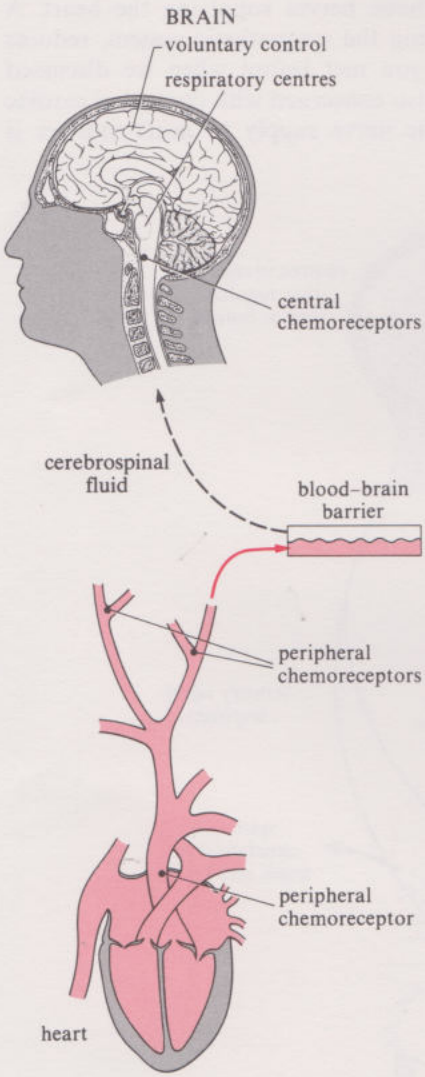


FIGURE 20 The basic components of the respiratory control system in humans.

6.3 NERVOUS CONTROL OF HEART BEAT

The need for effective control of cardiac output is very apparent if you think back to Sam, after his jog, in the TV programme. The blood *in the lungs* will be freshly loaded with oxygen and swept clear of CO_2. But to make use of these gas exchanges, there must be rapid circulation of blood to the tissues of the body where oxygen is needed, and respiratory CO_2 awaits removal. How is this achieved? Once again, we shall be looking for effectors, receptors and an intervening monitor and reference level.

Changes in cardiac output are primarily produced by alterations in the rate of contraction and the stroke volume of the heart. Cardiac output is also influenced by the contraction or dilation of the arterioles and arteries, but this discussion will focus on the heart as an effector.

NEURON

SENSORY NERVES

MOTOR NERVES

SYMPATHETIC NERVOUS SYSTEM

PARASYMPATHETIC NERVOUS SYSTEMS

STRETCH RECEPTORS

In breathing, there is a basic 'in-and-out' rhythm that is modulated according to need. There is a similar modulation of the rhythm of the heart. A totally excised heart—that is, one cut out of the body—will continue beating if it is bathed with the right kind of saline solution. Within the heart (in ways not discussed here), special fibres coordinate movements of the two atria and two ventricles in the standard sequence of muscular pumping. Modulation of that rhythm is achieved, as we shall see, by two distinct kinds of nerves.

Several of the control systems so far described depend on the transmission of information by nerve impulses. Information is coded in nerves in an electrical form. A single nerve cell—a **neuron**—carries electrical pulses of identical size and duration. It can be the time interval between pulses, or the patterning of the pulses or, indeed the presence or absence of pulses, that encodes information. Nerves that carry information from receptor to the monitor (in the brain) are termed **sensory nerves**. Those that travel from the brain are—if the effector is a muscle—termed **motor nerves**. As noted above, the mammalian heart exhibits a complexity that we have not met before: it is supplied by two kinds of motor nerve—one that stimulates it (part of the **sympathetic nervous system**) and one that inhibits it (part of the **parasympathetic nervous system**). The advantage of one system acting *antagonistically* to the other is that large changes in rate can be produced rapidly. For example, a small change in activity in each of the nerves will produce a large change in rate. A decrease in parasympathetic impulses increases heart rate and an increase in sympathetic activity also produces an increase in heart rate. (The 'beta-blockers' that you read about in Units 17–18 block the effect of the sympathetic nerves supplying the heart. A common drug, propranolol, by blocking the sympathetic system, reduces the heart rate.) The medulla (which you met before when we discussed control of breathing in Section 6.2) is also concerned with control of cardiac output. A simple representation of the nerve supply to heart muscles is shown in Figure 21.

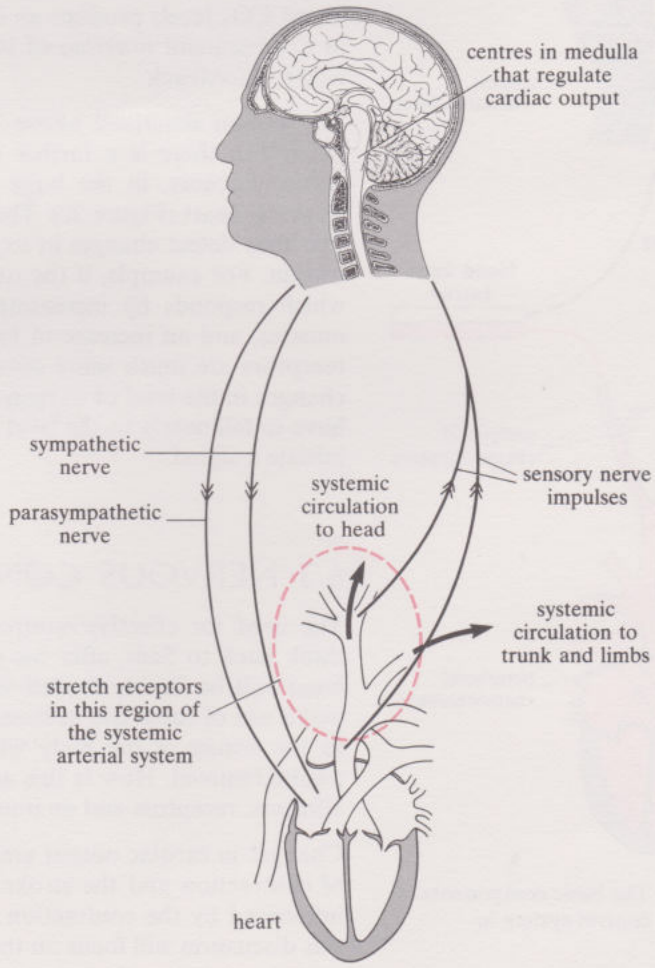


FIGURE 21 A simple representation of the nerve supply to the heart.

What kind of stimulus is detected in this system? You might reasonably expect raised CO_2 or lowered O_2 to have a stimulatory effect—both would then cause an increase in the heart rate during exercise. There is some evidence that chemoreceptors in the large arteries leaving the heart may play a minor part in the direct regulation of cardiac output. There is rather more evidence, however, that chemoreception of CO_2 has an indirect effect on the circulation by influencing the contraction or dilation of arteries and arterioles. Much more significant in direct heart beat regulation is the detection of *blood pressure*. In the aorta (the main artery leaving the heart carrying the systemic circulation, shown in Plate 9) and in the arteries leading to the head, there are special **stretch receptors** that detect changes in blood pressure.

□ In terms of homeostasis of blood pressure, would you expect a signal from stretch receptors (indicating rising pressure) to lead, via the monitor in the medulla, to sympathetic or parasympathetic stimulation of the heart?

■ Parasympathetic—leading to decreased heart rate, hence lowered pressure.

Thus, as described in this simplified outline, we have a homeostatic system for blood pressure. This time it depends on detection of pressure, modulation via a monitor (containing a reference level) in the medulla, and affected by the activity of the heart muscles. It relates easily to the metabolic needs of exercise. As noted earlier, CO_2 brings about dilation of the tissue arterioles, giving plenty of 'local blood' to supply oxygen and remove carbon dioxide. This dilation has the effect, of course, of lowering resistance to blood flow and so lowering blood pressure. And this, in turn is detected by the pressure receptors and so on.

Blood pressure homeostasis has important links with other control systems that you have already met. Various changes can occur *very rapidly* in the diameters of arterioles and arteries and have very marked effects on blood pressure—to which the heart must respond. For example, when the body is chilled, the blood supply to the capillaries in the skin is reduced. If blood is thus excluded from a significant proportion of the circulatory system, it is plain that, since the volume of blood is fixed, the pressure in the rest of the system will rise drastically unless the rate of heart beat is sharply reduced. This is achieved through the pressure homeostatic system: as pressure rises, stretch receptors are triggered, impulses pass down the parasympathetic nerves, and the heart rate slows.

We can usefully conclude this discussion with another foray into comparative physiology. Much of the early work on heart function was done on isolated frog hearts and, consequently, a good deal is known about the function of this organ. Although the frog heart resembles the mammalian heart in many ways, it has only one ventricle. The consequence of this is that oxygenated and deoxygenated blood mix in the ventricle. This may strike you as inefficient, but, as you will see, it is quite the reverse.

Think where frogs live. Their habitat is very wet. Because their skin is both thin and wet, oxygen can diffuse directly through to the bloodstream. Thus, the lung is not the only source of oxygen and, when the frog is underwater, the oxygen that the frog needs will come from the surrounding water via the skin. The advantage of having only one ventricle is now apparent. Blood from the skin that is rich in oxygen *can go directly to the tissues.* If the frog had a double circulation like that in mammals, the blood from the skin, already rich in oxygen, would then pass through the lungs for no purpose. As it is, the arrangement is ideal for the circumstances in which the frog lives.

Experiments with frogs have also provided further insights into heart function—as we shall show in Section 6.4.

ADRENAL GLANDS

ADRENAL CORTEX

6.4 HORMONAL CONTROL OF HEART BEAT

In an early physiological experiment, two frog hearts were set up in isolation (Figure 22). The only link between them was the circulating fluid. When the nerve to the first heart was stimulated by a mild electric current, the rate of beating altered, as you would expect. A much more surprising result was that the rate of the second heart also altered. The conclusion drawn was that there was chemical communication between the two hearts. Other experiments supported this conclusion, and eliminated other explanations, for example that the electrical signal passed through the circulating fluid. Thus, it was clear that one should look for a role for *hormones* in beat rate regulation.

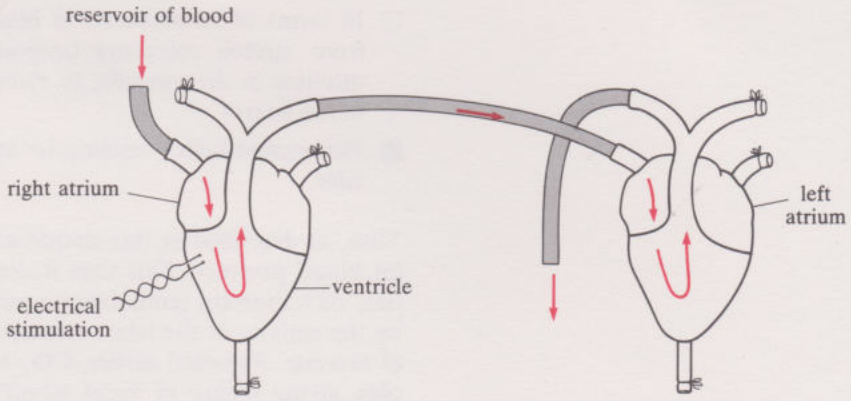


FIGURE 22 An early experiment in which two isolated frog hearts were connected together by tubing carrying a solution resembling blood. It demonstrated that, if one heart was stimulated electrically, a chemical in the fluid carried the signal for contraction from one heart to the other. The direction of movement of the solution is shown by the red arrows. Note that in the frog heart there is only one ventricle.

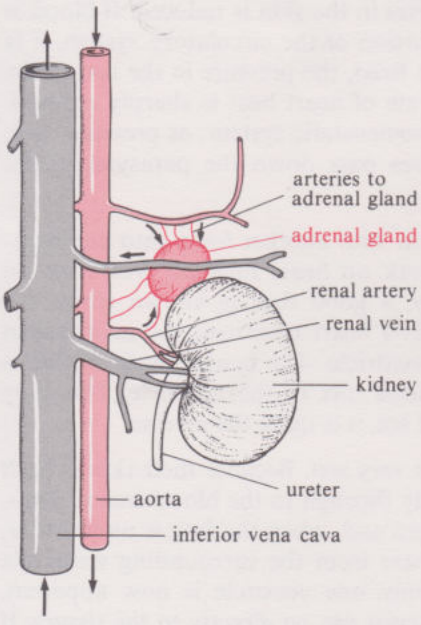


FIGURE 23 The position of the adrenal glands and the blood vessels supplying them, in a human.

You have already met the hormone adrenalin in Section 5.4. It is produced in the **adrenal glands**, two small pea-shaped organs situated close to the kidneys or directly attached to them (Figure 23). There are two layers of tissue in the adrenal glands: the outer **cortex** and the inner medulla. The hormone adrenalin can be extracted from the medulla, and when it is injected into animals or humans it produces a wide variety of effects: an increase in the rate of breathing, an increase in the heart rate, and increased glucose release from the liver. In addition, there is an increase in resistance to blood flow in the skin, caused by the reduction of blood flow to the skin capillaries, leading to the typical paleness of shock. Also, there is, in humans, a feeling of anxiety. All these physiological responses occur also when the body is subjected to sudden stress, such as fright.

When the brain is stimulated by stress, a signal is sent via the sympathetic nervous system to the adrenal glands. Adrenalin is stored in the tissue of the glands in the form of inert granules, and the signal causes the start of release of active hormone into the bloodstream. When the hormone is in the bloodstream, it passes through the heart, and also enters the heart's own blood supply—the coronary blood vessels which supply the heart muscle with oxygen, glucose, etc. (Figure 9b). Thus adrenalin is delivered directly to its site of action—the heart muscle. Here, it mimics the action of the sympathetic nervous system.

What is its effect on beat rate?

It causes faster and stronger contraction of the muscle, by increasing both heart rate and stroke volume, and cardiac output is increased, initially overriding the nervous control. When the stress is passed, and adrenalin release has ceased, the levels of adrenalin in the blood fall. The fall is due to the action of enzymes that continually catalyse the breakdown of adrenalin in blood and tissues, to prevent it from continuing to stimulate the body after the need for it has passed.

ITQ 9 Is the release of adrenalin under conditions of stress a homeostatic response? Give reasons for your answer.

From the answer to ITQ 9, it is clear that adrenalin is quite unlike a homeostatic hormonal such as insulin. Adrenalin is released in response to stress, and it has a wide range of physiological effects. It is possible to determine experimentally the types of stress that produce adrenalin release, and it is also possible to measure how much adrenalin is released in these varying conditions. The blood test has to be quite sensitive since an injection of a very small quantity—about $0.2\,\mu g\,l^{-1}$ of adrenalin—produces quite a large heart rate response. As a result of such measurements, we know that adrenalin is released in response to:

1 physical exertion
2 exposure to cold
3 reduction in blood pressure
4 reduction in blood flow to the brain
5 hypoglycaemia
6 anaesthetic drugs
7 emotional states such as fright

All the physiological effects of adrenalin that we have mentioned tend to counteract the seven kinds of stress listed above.

SUMMARY OF SECTION 6

1 The survival of organisms depends upon efficient coordination of physiological processes.

2 Homeostatic mechanisms maintain the organism in an appropriate state: they act to restore stability by negative feedback.

3 Information about the state of the organism is acquired by receptors and passed to effectors.

4 In mammals, the oxygen level of the blood is maintained by a combination of adjustment of blood flow and breathing.

5 Information about the gas content of the blood is acquired by central and peripheral chemoreceptors.

6 Breathing rate and heart rate have natural rhythms that are modulated by the brain on the basis of information received from receptors.

7 The heart receives signals from both the sympathetic and the parasympathetic nervous systems. The signals act antagonistically to produce a high degree of control of heart rate, and a rapid response.

8 Adrenalin, released from the adrenal glands near the kidney, stimulates the heart to increase rate and stroke volume. It also generally increases the state of preparedness of the body for rapid action.

SAQ 8 Describe the possible physiological consequences of going swimming off Brighton beach on Christmas Day, and then coming ashore and swallowing a large brandy (or two). (*Hint* Think about what would happen to the blood vessels in the skin, since one of the actions of alcohol is to dilate blood vessels.)

SAQ 9 Figure 24 shows the relation between the rate of heat loss by sweating and body temperature for a woman with a slight fever (dotted line) and a woman in normal health (dashed line), under controlled conditions. Body temperature has been measured by monitoring the temperature at the carotid artery in the neck. Which *one* of the following deductions can reasonably be made from the graph?

(a) The fever causes the small capillaries in the skin to narrow in diameter.
(b) The fever alters the activity of the sweat glands so that they secrete more sweat.

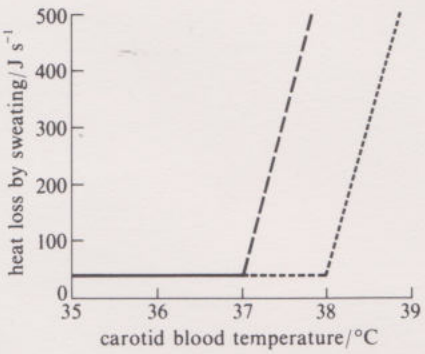


FIGURE 24 Figure for SAQ 9.

(c) The fever alters the temperature at which the hypothalamus initiates sweating.
(d) The effect of the fever is to reduce the heart rate, and so reduce the blood flow through the skin.

SAQ 10 How do the differences in the structure of the heart between mammals and frogs relate to the supply of oxygen to the tissues?

7 CONCLUSION

The preceding pages have considered the regulation of body temperature, blood glucose level, breathing, and cardiac output. In the last of these, the effect of adrenalin in stimulating the heart to sudden high levels of activity was non-homeostatic. All the other processes involve negative feedback and hence homeostasis. In all of them, a changing level of some attribute (glucose level, temperature) is detected by receptors which, after comparison with some reference level in the monitor, leads to an alteration in effector activity in the direction of countering the perceived change. These are common features in all homeostatic systems. Apart from differences in detail, the only major way in which one homeostatic system may differ from another is in the nature of the signal—which may be hormonal (as in glucose regulation) or nervous (as in temperature regulation).

In this Unit we have looked at a number of physiological systems in animals, and considered their function as part of the whole organism. Although we have described a very varied group of systems, they all have the same role: that of maintaining the internal environment. They act to keep physiological and biochemical events within a tolerable range.

This is not a novel way of looking at the natural world; it was established by Claude Bernard, a French physiologist, in the 19th century (Plate 11). He formulated his ideas during a study of the role of the liver as a glycogen store. So although he did not himself invent the term homeostasis, he is rightly remembered as the originator of the homeostatic systems approach to the study of physiology—the approach we have followed throughout this Unit.

Although, working in the 19th century, Bernard could not have known it, a great many physiological processes are influenced by enzymes and other proteins such as haemoglobin, insulin and many more. This leads us back to a matter of great importance—the link between genes, metabolic proteins and, in turn, to the overall physiology of an organism. That link, a closer exploration of 'DNA makes RNA makes protein', is the subject of Unit 24.

OBJECTIVES FOR UNIT 23

After you have worked through this Unit, you should be able to:

1 Explain the meaning of, and use correctly, all the terms flagged in the text.

2 Describe the supply of oxygen to cells in animals and recognize the limitations on size imposed by the lack of a circulatory system. (*SAQs 1 and 2*)

3 Describe the supply of oxygen and respiratory substrates to the cells in mammalian tissues, and the removal of waste products. (*ITQs 1–4; SAQ 4*)

4 Describe the circulation of blood through the heart and lungs of a mammal and distinguish between the structure and function of veins and arteries. (*ITQ 5; SAQ 3*)

5 Explain the role of blood cells in the transport of dissolved gases. (*SAQ 5*)

6 Outline the effects of diabetes, and explain how blood sugar levels can be controlled in this disease. (*SAQ 6*)

7 Distinguish in general terms between amphibian and mammalian circulatory systems. (*SAQ 9*)

8 Identify the key features of control mechanisms and explain the difference between homeostatic and non-homeostatic mechanisms. (*ITQ 6–8; SAQ 10*)

9 Give an account of the control mechanisms involved in maintaining homeostasis in the following mammalian systems:

(a) thermoregulation system (*ITQs 7 and 8*)
(b) glucose supply (*SAQ 7*)
(c) heart and circulatory system (*SAQ 8*)

FURTHER READING

For an introduction to comparative animal physiology, we suggest that you read:

Wood, D. W. (1983) *Principles of Animal Physiology*, Edward Arnold.

Human physiology is covered very well, though at a higher level than in this Unit, in a series of books called *Physiological Principles in Medicine*. (The series is still being expanded.) Particularly relevant to this Unit are:

Sandford, P. A. (1982) *Digestive System Physiology*, Edward Arnold.

Widdicombe, J. and Davies, A. (1983) *Respiratory Physiology*, Edward Arnold.

Hardy, R. N. (1982) *Endocrine Physiology*, Edward Arnold.

For a very well illustrated textbook that covers most of the biology in S102 in detail, we recommend:

Starr, C. and Taggart, R. (1987) *Biology, The Unity and Diversity of Life*, Wadsworth Publishing Co.

ITQ ANSWERS AND COMMENTS

ITQ 1 45 beats min^{-1}. In one second there would be $30/40 = 0.75$ beats. So in 60 seconds there would be 60×0.75 beats, so the heart rate is 45 beats min^{-1}.

ITQ 2 The pulse is a repetitive event consisting of the pulse you feel plus the space between the pulses. To get thirty complete cycles of pulse and 'space' you need to count from the instant you feel pulse 1 to the instant you feel pulse 31. You then have thirty pulses and thirty spaces.

ITQ 3 The stroke volume was about 150 cm^3. Using Equation 2, the calculation is:

$$\text{stroke volume} = \frac{\text{cardiac output}}{\text{heart rate}}$$

$$= \frac{25 \text{ litres min}^{-1} \times 1\,000 \text{ cm}^3}{170 \text{ beats min}^{-1}}$$

$$\approx 150 \text{ cm}^3$$

Athletes train hard and develop powerful muscles. The training also affects the heart muscle, and athletes can achieve the same cardiac output as an untrained person, but with a slower heart rate. This is why the figures in this example differ from those given in the text for a relatively fit person.

ITQ 4 (a) The dye circulates through the bloodstream and is gradually diluted. It is not instantly dispersed throughout the blood. So the first peak represents the dye passing the sample point during the first complete circulation. The level falls, only to rise again during the second circulation. The second peak would be lower as the dye is by then more dispersed in the blood.

(b) The peak in the exercise curve occurs earlier because blood is circulating faster and therefore the dye travels round the blood system and reaches point S more quickly. During exercise, heart rate and stroke volume increase.

ITQ 5 About 4.9 litres min^{-1}. You were told that the mean dye concentration was 1.6 mg l^{-1}. Since 5 mg was injected, the volume of blood that contained the dye was $5/1.6 = 3.13$ litres. Extending the slope of the resting curve to the horizontal axis shows that the dye takes 38.5 seconds to pass through the heart once. So 3.13 litres circulates in 38.5 s. It follows that $(3.13/38.5) \times 60$ litres circulates in one minute. This is about 4.9 litres min^{-1}.

ITQ 6 The human body loses water through several main routes:

(a) During breathing water is lost by evaporation from the linings of the nose, lungs, and mouth.

(b) Water is lost via the skin by sweating.

(c) The body discards waste, and loses water as it does so. Urination may be a way of getting rid of excess water, but urine also has the function of removing nitrogen from the body.

ITQ 7 The completed passage should read as follows:

In the heating system in Figure 16, a change in temperature is detected by the thermostat. The latter is termed the *receptor* because it receives information about the temperature of the room. In this particular control system, the thermostat also contains the pre-set *reference level*. A *signal* passes from this point to the *monitor*. This compares the incoming information with its internal instructions, and, as a consequence, sends a *signal* to the *effector*. This is switched on, so heating the room. Eventually the temperature increases to the point at which the *reference level* is exceeded. When this happens, the *effector* is switched off via the control system, so preventing any further rise. This is an example of *negative* feedback.

ITQ 8 The labelled parts of the regulatory subsystem shown in Figure 17b are:

(a) signal (nerve impulse);
(b) monitor and reference level;
(c) signal (nerve impulse);
(d) signal (nerve impulse);
(e) receptor;
(f) effector;
(g) effector.

ITQ 9 The release of adrenalin in response to stress is not a homeostatic response. In this situation a temporary increase in the level of circulating adrenalin leads to a number of temporary adjustments of the body's physiology, which all contribute to overcoming stress, or help survival in an emergency. The action of adrenalin is to produce an unstable state rapidly, but temporarily. There is a subsequent restoration of homeostasis by other means.

SAQ ANSWERS AND COMMENTS

SAQ 1 (a) has the larger concentration gradient. In both (a) and (b) the cells are the same. So the concentration difference between each cell and the pondwater is the same. However, the distances are different. The greater the distance from the pondwater, the smaller the concentration gradient. So (a) has the larger concentration gradient.

SAQ 2 (a) will have the larger diffusion rate. Both cells are the same distance from the pondwater, but that in (a) is metabolizing much faster than that in (b), which has very few mitochondria. Therefore the oxygen concentration difference will be greater in (a), the concentration gradient will be larger and so the diffusion rate will be greater.

SAQ 3 (b) and (d) are true.

(a) is false because the pulmonary artery carries blood to the lung. This blood has been carried to the heart from the tissues and, having given up oxygen, it has collected carbon dioxide to be disposed of.

(b) is true because most veins bring blood from tissues, where oxygen will have been used, back to the heart. An exception is the pulmonary vein, which carries oxygen-rich blood.

(c) is false because all blood has to pass through both heart and lungs.

(d) is true because the two routes through the heart are independent. There is a true double circulation.

SAQ 4 In Unit 22 you saw that it was possible to generate ATP by glycolysis in the absence of oxygen. The stepping exercise in the experiment should have been sufficiently strenuous to cause you or your assistant to generate ATP from anaerobic respiration. One of the consequences of exercise is a build-up of lactate—the oxygen debt (Unit 22, Section 6.4). The oxygen required to pay off this debt comes from the increased cardiac output being maintained after exercise, only returning to normal when the debt is paid off. Lactate accumulation makes muscles feel tired.

SAQ 5 It is advantageous for blood to have a low viscosity because it travels through vessels of very narrow diameter. The thicker blood is, the more pressure is required to force it through a narrow tube of a given diameter and the greater the resulting load on the heart. Imagine the difference between forcing water out of a syringe needle, and forcing treacle out of the same syringe. The treacle would require more pressure—indeed, you might crack the syringe.

SAQ 6 Injection of too much insulin would promote glucose transfer out of the blood into cells. The blood glucose level would fall, and the person would have hypoglycaemia. If they could recognize the symptoms, they could rapidly raise the blood sugar level by eating glucose in the form of tablets, or sweets or any sugar-rich food.

SAQ 7 During exercise there is a build-up of lactate in the muscles and the bloodstream. Lactate is reconverted into pyruvate in the muscle, but the liver also takes up lactate from the bloodstream and converts it back to glycogen.

SAQ 8 A Christmas swim at Brighton is likely to be a somewhat chilly experience. The natural reaction of the body to cold would be to constrict the surface capillaries to reduce peripheral blood flow and hence heat loss. However, the over-riding effect of alcohol will be to dilate the blood vessels, allowing a greater flow of warm blood through the skin giving a pleasant feeling of warmth. The heart rate will probably increase as a result of both the exercise (swimming hard) and the shift of blood from the centre of the body to the periphery. However, the feeling of well-being would be illusory, for the body would be shunting heat away from the centre towards the skin where loss to the cold air would be rapid.

SAQ 9 (c) is the correct answer. The only reasonable deduction that can be made from the data is that the reference point in the hypothalamus is shifted in the woman with the fever. The two curves are identical apart from the set temperature at which sweating starts, which is one degree higher in the woman with the fever.

(a) No information is given about capillary size, but you should expect the capillaries to carry more blood as temperature rises. This is because the arterioles feeding the capillaries would expand.

(b) This is likely to be true, but you cannot make such a statement on the basis of the graph.

(d) There is no information about heart rate in the graph, but the slopes of the two curves are identical, which suggests that there is no difference in the rate of heat loss.

SAQ 10 Both frogs and mammals have blood that carries oxygen, lungs and a heart that circulates the blood. In the frog's heart, there is only one ventricle, whereas in mammals there are two. The consequence is that the blood in the frog ventricle is a mixture—some of it has come through the lungs, some of it has arrived via the skin. Frogs normally live in wet environments and their skin can absorb oxygen by diffusion from the wet surface through into the blood capillaries. So, the undivided ventricle of the frog is consistent with its semi-aquatic life-style. Underwater, it can obtain oxygen from the water through its skin and lungs provide no oxygen; on land drying of the skin can be tolerated as oxygen is supplied by the lungs.

INDEX FOR UNIT 23

ADP, 4
adrenal cortex, 36
adrenal glands, 36
adrenalin, 27, 28, 31, 32, 36, 37
air, oxygen in, 4, 8, 10
alveoli, 9, 10, 11, 13, 14, 24
amino acids
 catabolism of, 23
 transport of, 11
ammonia, excretion of, 23
antagonistic action of nervous systems, 34
aorta, 14, Plate 9
arteries, 12, 13, 14, 33
 chemoreceptors in, 33
arterioles, 12, 14, 19–20, 33, 35
ATP, 4
atria, 12, 13, 14, 34, Plate 9
autotrophs, 4

Bernard, Claude, 38, Plate 11
beta-blockers, 34
β-oxidation pathway, 26
bicarbonates formed during catabolism, 21–2, 24
birds
 body temperature, 24
 excretion, 23
 oxygen supply, 8–9, 10, 12
bladder, 23
blood system, 8, 10, 20, 24
 blood cells and haemoglobin, 18–20, Plate 10
 exercise and, 15–18, 20, 32, 33
 heart and, 12–14
 oxygen transport in, 11–12, 32–3, 37
 pressure, 35
 see also glucose levels
brain
 control systems in, 31, 32–4
 glucose needed for, 24, 26
breathing, 8–9, 10
 control mechanisms of, 32–3, 34, 37
 see also respiration
bronchi and bronchioles, 9–10

capillaries, 12, 21
carbohydrates, digestion of, 25
carbon dioxide
 removal of, 21–2, 24
 transported in blood, 11, 13, 18, 32–3, 35
carbonic anhydrase, 21
cardiac output, 12, 20
 and control mechanisms, 32, 33, 34–5, 36, 37
 measuring, 15–18
catabolism, 4, 9, 11
 of amino acids, 23
 of fats, 26, 27
 products of, removing, 11, 22–4
catalysis
 of enzymes, 36
 in red cells, 20, 24
cells
 blood, 18–20, Plate 10
 see also multicellular; single-celled
central heating system, control of, 28–9
cerebellum, 32
cerebral cortex, 33
cerebrospinal fluid, 33
chemoreceptors, 33, 35, 37
chloride ions, excreted, 26
cilia, 11
circulatory systems, 10–21, 34
 see also blood system
clotting mechanism, 18, 20
colorimeter, 17
concentration gradient, 6, 10, 22
control mechanisms, 28–38
 of blood glucose level, 31–2
 of breathing, 32–3, 34, 37
 of heart beat
 hormonal, 35–7
 nervous, 33–5, 37
 see also under temperature
co-ordination, 4
coronary blood vessels, 13, 14
cortex
 adrenal, 36
 cerebral, 33
Cyanea (jelly-fish): oxygen supply, 7–8

deamination, 23
dehydration, 26
diabetes, 26, **27**
diaphragm, 10
diffusion of oxygen, **6**
 see also under oxygen supply
digestion of carbohydrates, 25
double circulation, 13, 20

effectors, 28, 31, 33, 37
energy, 14
 see also glucose
enzymes
 catalysis of, 36
 destroying insulin, 27
 in red cells, 20, 24
evolution by natural selection, 14, 21
exercise and blood system, 15–18, 20, 32, 33
extracellular fluid, 6

fats
 catabolism of, 26, 27
 transport of, 11
fish
 excretion, 23
 oxygen supply, 8–9, 10
flatworm: oxygen supply, 6–7, 10
flea: oxygen supply, 8
flow diagram of heating system, 28, 29
food and glucose level in blood, 25, 26
frog hearts, 35–6
fructose, 25
function and structure, relationship between, 14, 21

gills, 8–9, 10
glands, 31, 32, 36
 see also hormones
globin, 19
glucagon, 27, 28, 31, 32
gluconeogenesis, 26, 27
glucose levels in blood, 11, 14, 24–8
 control of, 31–2
 low and high, 26, 28
 regulation of, 25, 27
glycerol, 26
glycogen, 24, 25, 38
 breakdown to glucose, 26, 27, 28
glycogenolysis, 26, 27, 28

haem, 19
haemocyanin, 12
haemoglobin, 11, 18–22
heart, 12–14, 20
 beat, control of
 hormonal, 35–7
 nervous, 33–5, 37
 blood system and, 12–14
 effect of exercise on, 15–18, 20
 frog's, 35–6
 pig's, 12, Plate 9
heat transfer in body, 11, 23–4
 see also temperature
hepatic portal vein, 25
'Hering–Breuer reflex', 33
heterotrophs, 4
high glucose levels in blood, 26
homeostasis, 28, 29, 31–2, 35, 37, 38
hormones, 26
 and blood glucose level, 27, 28, 31–2
 circulation of, 11
 and control of heart beat, 35–7
hydrogen ions, 22
hyperglycaemia, 26, 27, 32
hypoglycaemia, 25
 hormone *see* insulin
hypothalamus, 31

infection, protection against, 18
insects: oxygen supply, 8, 10, 12
insulin, 27, 28, 31, 32
internal body temperature, 23–4
intestines, 25
ions, 22
 excreted, 26
iron in haemoglobin, 19, 20

jelly-fish: oxygen supply, 7–8

kidneys
 adrenal glands near, 36, 37
 and elimination of wastes, 23, 24, 26
 glucose reabsorbed in, 25
kinetic energy, 14

lactate, synthesis of, 26, 27
liquids and oxygenation *see* blood; water
liver
 blood supply to, 25
 glucose converted in, 24, 26, 27, 38
low glucose levels in blood, 26
lungs, 8–9, 10, 11, 13, 21, 22, 24, 32, 33

mammals
blood supply, 37
body temperature, 24
heart, 34
oxygen supply, 8–9, 10, 12
medulla (of brain), **32**, 33, 34, 36
metabolism, removing products of, 21–4
carbon dioxide, 21–2
heat transfer, 23–4
water and nitrogen compounds, 22–3
mitochondria, 26
oxygen supply, 4, 5, 6
monocytes, Plate 10
monitors, **28**, 31, 34
motor nerves, **34**
multicellular organisms, oxygen supply in
large, 8–10
small, 6–8
muscles, 27
and breathing, 10
see also heart
glucose conversion in, 24, 26

natural selection, evolution by, 14, 21
negative feedback, **29**, 31, 33, 37
nervous system
and control of heart beat, 33–5, 37
control mechanisms and, 33, 34–5, 37
glucose needed for, 26
neuron, **34**
nitrogen compounds eliminated, 22–3, 24

oxidation, 4, 26
see also oxygen supply
oxygen supply, 4–10
diffusion of, 4–6, 7, 8, 9, 10, 24, 35
transport in blood system, 11–12, 32–3, 37
in large multicellular organisms, 8–10
in small multicellular organisms, 6–8

pancreas, **32**
parasympathetic nervous system, **34**, 35, 37
photosynthesis, 4
physiology, 4
see also circulatory systems; control mechanisms; glucose levels; metabolism; oxygen supply
pig's heart, 12, Plate 9
pituitary, 32
plasma, **11**, 18, 19, 20, 22, 24, 33
platelets, **18**, 20, Plate 10
pons, **33**
positive feedback, **29**
pressure
blood, 35
water, solubility of oxygen and, 5
principles of regulation *see* control mechanisms
proteolytic (protein-destroying) enzymes, 27
pulmonary artery, 13, Plate 19
pulmonary circulation, **13**, 20
pulmonary vein, 13, Plate 9

receptors, **28**, 31, 33, 34, 37
stretch, 35
red cells, 11, **18**, 19, 20, 21, 22, 24, Plate 10
and glucose, need for, 26
reference levels, **28**, 31
regulation, 4
principles of *see* control mechanisms
reptiles: excretion, 23
respiration, 21–2
see also breathing; oxygen supply

salts in solution, 5, 18
sensory nerves, **34**
signals, **28**, 31, 32, 33
single-celled organisms: oxygen supply, 5–7, 10
sodium ions, excreted, 26
solution, 18
oxygen in, 5, 7, 8, 9, 10, 35
spinal cord, 32, 33
spiracles, **8**
stored energy, 14
strain energy, 14
stress, adrenalin release produced by, 36
stretch receptors, 34, **35**
stroke volume of heart, **16**, 20, 33, 36, 37
structure and function, relationship between, 14, 21
substrate, metabolic *see* glucose
sympathetic nervous system, **34**, 37
systemic circulation, 13, **14**, 20, 34

tape-worm: oxygen supply, 6
target tissue, **26**, 28
teleological statements, **14**, 21
temperature
control of
internal, 23–4, 30–1
in central heating systems, 28–9
heat transfer in body, 11, 23–4
and solubility of oxygen in water, 5
thermoregulatory systems *see* temperature control
trachea, 9, 10
tracheal system, **8**, 10

unicellular *see* single-celled
urea, **23**, 26
uric acid, 23
urine, 23, 24, 25, 26

veins, **12**, 13, 14, 19–20
hepatic portal, 25
vena cava, **13**, Plate 9
ventricles, **12**, 13, 14, 34, Plate 9
viscosity of blood, **20**, 21
voluntary control of breathing, 33

water
loss, 26
oxygen diffused in, 5, 7, 8, 9, 10, 35
as product of metabolism, removing, 22–3, 24
white cells, **18**, 20, Plate 10

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Figure 6 Barrington, E. J. W., *Invertebrate Structure and Function*, 1979, Nelson and Sons; *Figure 12(b)* Keele, C. A., Neil, E. and Joels, N., *Samson Wright's Applied Physiology*, 1982, Oxford University Press.

Plate 10 Wheater, P. R., Burkitt, H. G. and Lancaster, P., *Colour Atlas of Histology*, 1985, Longmans; *Plate 11* Wellcome Institute Library, London.

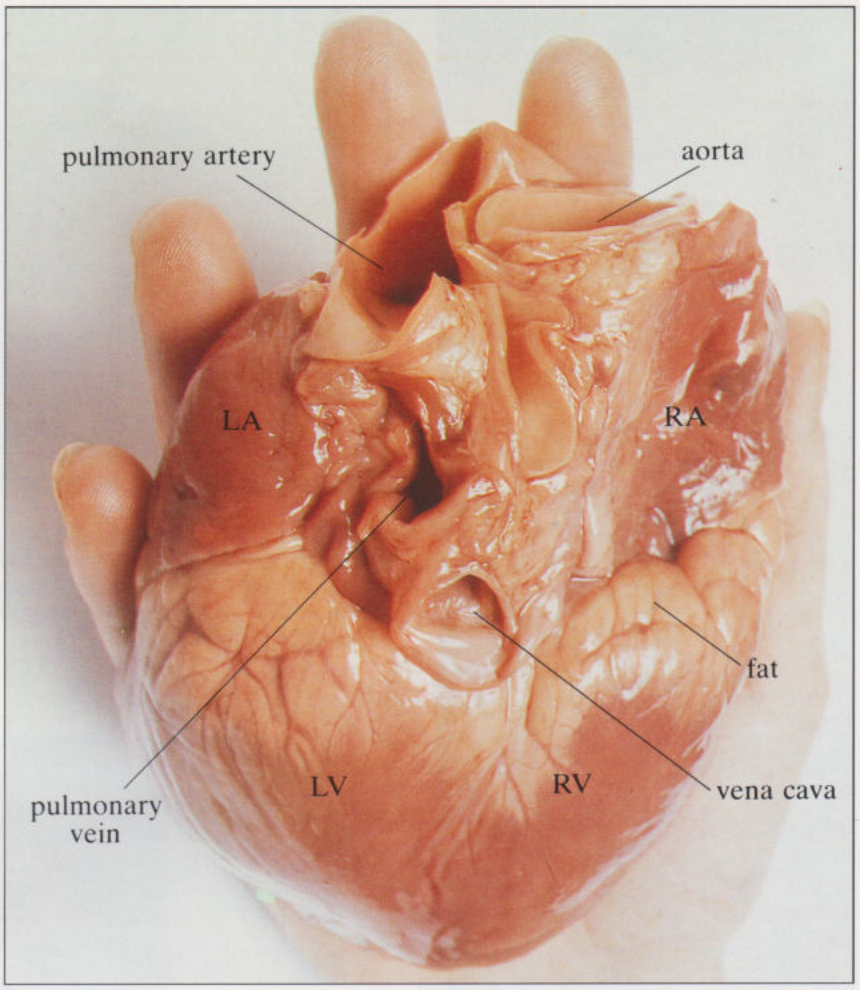


PLATE 9 Dorsal view of the heart of a pig. The diameter of the pulmonary arterial wall appears larger then usual, partly as a result of the angle of the heart and partly because the pulmonary artery had been slashed. The ventricles are foreshortened because of the angle at which the picture was taken. LA, left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle. Note the cushioning layer of fat round the bottom of the heart.

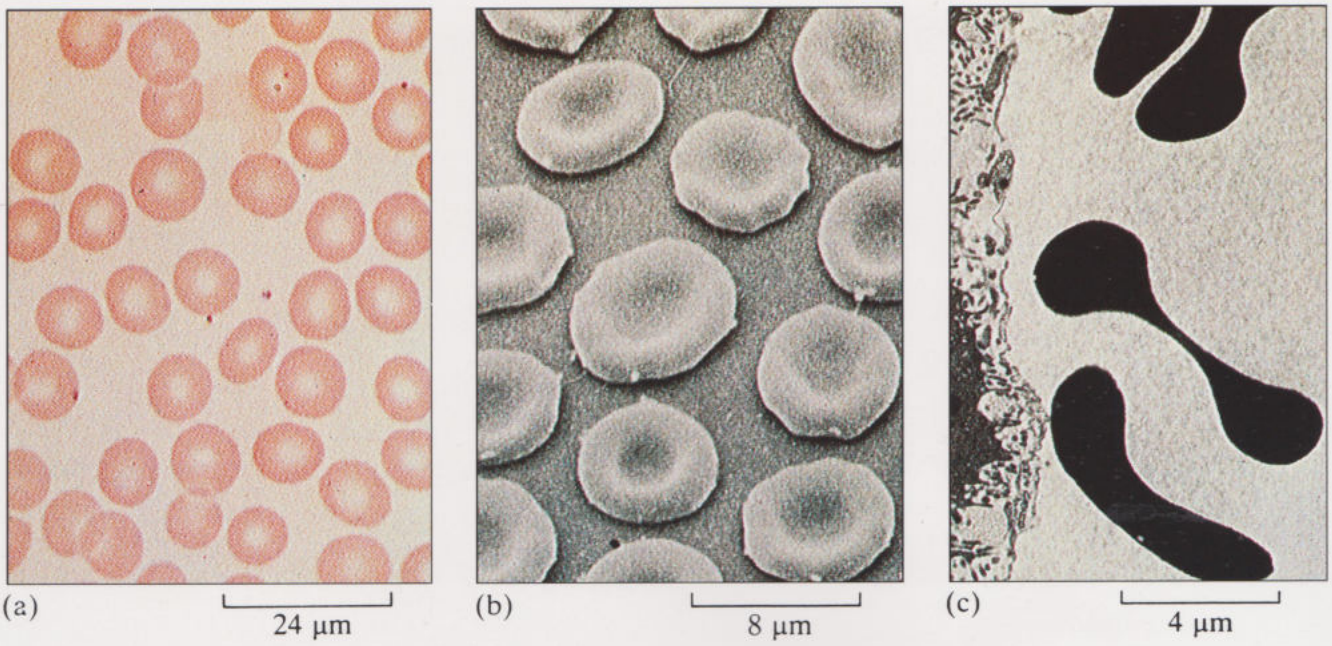


PLATE 10 Human blood. (a) Red cells. Note that they do not have a nucleus. (b) Scanning EM photograph of red blood cells. (c) Section through red cells. (d) Blood platelets. (e) White blood cells. There are several types of white cell. These cells are lymphocytes, which are concerned with response to infection. (f) These cells are monocytes, the largest of the white blood cells. They swallow debris and foreign bodies in the blood.



PLATE 11 The French physiologist Claude Bernard giving a practical demonstration in physiology to his pupils (oil painting by an unknown artist, in the collection in the Wellcome Institute for the History of Medicine).